Rhodium-Catalyzed Ring-Opening Reaction of Cyclopropenes. Control of Regioselectivity by the Oxidation State of the Metal

Albert Padwa,* Jamal M. Kassir, and Simon L. Xu

Department of Chemistry, Emory University, Atlanta, Georgia 30322

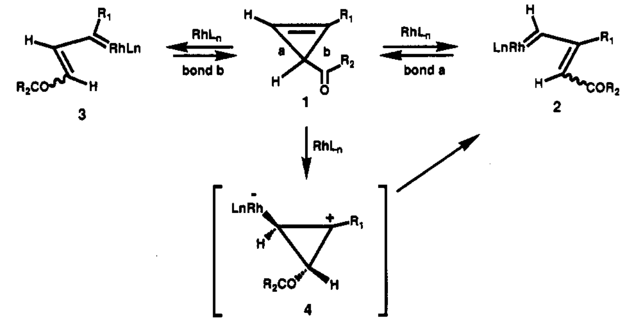
Received September 17, 1991

Summary: The Rh(II)-catalyzed reaction of unsymmetrically substituted cyclopropenes gives substituted furans derived from cleavage of the less substituted σ-bond. In contrast, Rh(I) catalysis results in cleavage of the more substituted σ-bond producing a regioisomeric set of furans.

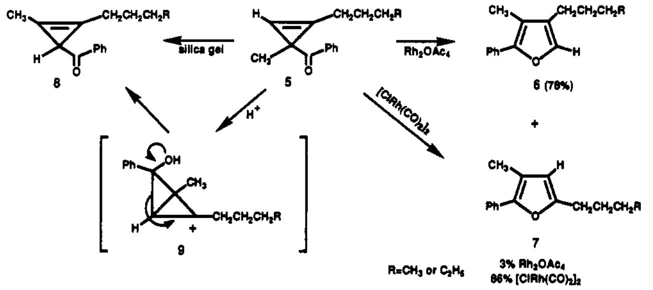
The interaction of transition-metal complexes with strained carbocyclic compounds has been a subject of considerable interest in recent years.[1-4] These metals catalyze a variety of rearrangements, the course of which depends on the nature of both the substrate and the metal complex.[5] Among these, the rhodium(II)-catalyzed ring opening of cyclopropene derivatives occupies a uniquely important position due to its synthetic as well as theoretical interest.[6-10] Moreover, the catalytic transformations encountered using binuclear rhodium compounds are often highly chemo-, regio-, and stereoselective processess.[11,12] Recent reports concerning the Rh(II)-catalyzed isomerization of cyclopropenes by Doyle and Müller[11] and the double alkyne insertion reaction of α-diazo ketones by Hoye and Dinsmore[12] prompt us to communicate our results in related studies. We describe herein our findings that the ring cleavage reaction is highly regiospecific and that the product composition is markedly dependent upon the oxidation state of the metal.

The Rh(II)-catalyzed ring opening of an unsymmetrically substituted cyclopropene such as 1 may lead to two regioisomeric rhodium–carbene complexes, each of which can exist as an E/Z set of stereoisomers. However, in all cases studied to date, the major products were always derived from cleavage of the less substituted cyclopropene bond (i.e., bond **a**).[6-12] The Doyle/Müller proposal[11] accounts for these observations by invoking a preferential electrophilic attack by the bulky Rh(II) catalyst trans to the ketone moiety, producing the more substituted cyclopropyl cation 4 (Scheme I). Disrotatory ring opening of 4 leads to the carbene complex 2. Rapid equilibrium among all the stereo- and regioisomeric vinyl carbenoids was also suggested to be a factor in determining the regioselectivity of bond cleavage.[11]

Scheme I



We have found that treatment of 2-diazo-1-phenyl-1-propanone with 1-hexyne and Rh_2OAc_4 in benzene at 80 °C afforded a 22:1 mixture of furans 6 and 7 in 82% overall yield. The structural assignment rests on the location of the furanyl proton in the NMR spectrum.[13] By carrying out the reaction at 25 °C for only 15 min, it was possible to isolate the putative cyclopropene 5 in 75% yield. It is interesting to note that silica gel chromatography of 5 resulted in quantitative isomerization to cyclopropene 8, a transformation which presumably proceeds via the intermediacy of the bicyclo[1.1.0]butane cation 9. Further treatment of 5 with Rh_2OAc_4 afforded furans 6 and 7 in the same ratio as previously encountered with the diazo compound. The regiochemical outcome is perfectly compatible with the earlier findings.[11,12] *Replacement of Rh_2OAc_4 with a rhodium(I) catalyst* (i.e., *$[ClRh(CO)_2]_2$*) *resulted in a pronounced alteration in the ratio of furans.* Thus, a solution of 5 in CH_2Cl_2 with 2 mol% of $[ClRh(CO)_2]_2$ reacted very cleanly at 25 °C to give exclusively furan 7 (86%) which corresponds to the minor product (3%) derived from the Rh(II) reaction. No signs of furan 6 (<2%) could be detected in the crude reaction mixture by NMR spectroscopy. An analogous set of results was also obtained using 1-heptyne ($R = C_2H_5$).



When the α-methoxy group of the keto cyclopropene is replaced with hydrogen (i.e., 10), a dramatic change in the course of the reaction was observed. Thus, treatment of 10 with 2 mol % Rh_2OAc_4 in benzene at 80 °C gave furans 11 and 12 (3:1 mixture) in only 6% yield.[14] The major

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[12] Hoye, T. R.; Dinsmore, C. J. *Tetrahedron Lett.* **1991**, 3755.

[13] Compound 6: NMR ($CDCl_3$, 300 MHz) δ 0.95 (t, 3 H, $J = 7.3$ Hz), 1.42 (sex, 2 H, $J = 7.3$ Hz), 1.50–1.60 (m, 2 H), 2.19 (s, 3 H), 2.39 (t, 2 H, $J = 7.3$ Hz), 7.20 (s, 1 H), 7.26–7.66 (m, 5 H). Compound 7: NMR ($CDCl_3$, 300 MHz) δ 0.94 (t, 3 H, $J = 7.2$ Hz), 1.42 (sex, 2 H, $J = 7.2$ Hz), 1.65 (q, 2 H, $J = 7.2$ Hz), 2.24 (s, 3 H), 2.63 (t, 2 H, $J = 7.2$ Hz), 5.93 (s, 1 H), 7.18–7.58 (m, 5 H).

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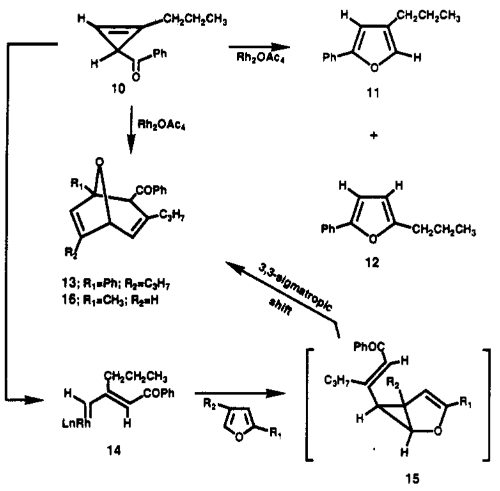
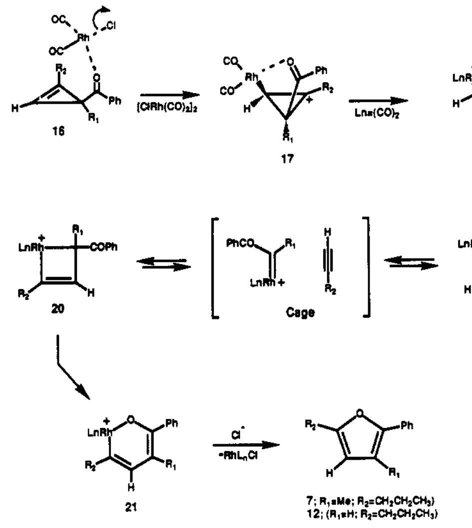


product isolated (52%) corresponded to oxabicyclo[3.2.1]octadiene **13**, whose formation is easily rationalized by proposing a secondary intermolecular addition of the expected vinyl carbenoid **14** onto the π-bond of furan **11** followed by a 3,3-sigmatropic rearrangement.[15] The bimolecular addition reaction only occurs with furan **11** due to its more reactive π-bond.[15] Supporting this hypothesis, the reaction of **10** with 1 equiv of 2-methylfuran produced the related oxabicyclic **16** in good yield. It is obvious that the presence of a hydrogen atom at the 3-position of the cyclopropene ring has dramatically affected the course of the reaction. The high yield of **13** from cyclopropene **10** can be attributed to the preferential generation of the (*E*)-vinyl carbenoid **14**, whose formation is undoubtedly related to steric factors. The less stable *Z* isomer is sterically destabilized by interaction of the acetate ligands of the catalyst and the larger benzoyl group. Since the carbenoid center of **14** cannot easily cyclize onto the oxygen atom of the ketone,[16] it either reverts back to starting material or reacts with furan **11** to give **13** in high yield. Oxabicyclic ring formation was not observed with the corresponding methyl-substituted cyclopropene **5**, probably because much more of the *Z* vinyl carbenoid is formed and cyclization to the furan occurs readily from this stereoisomer. It should be noted that the *rhodium dicarbonyl chloride dimer promoted opening of 10 was extremely specific producing only furan 12 in 86% yield.* No trace of either **11** or **13** could be detected in the crude reaction mixture by NMR spectroscopy.

Our mechanistic rationale to account for the Rh(I)-catalyzed transformation is shown in Scheme II. Electrophilic attack of $[ClRh(CO)_2]_2$ on the less substituted carbon of the cyclopropene π-bond affords the tertiary cyclopropyl carbocation **17**. Ring opening followed by a rapid electrocyclization reaction produces the metallocyclobutene **19**. Equilibration of **19** with the thermodynamically more stable 1,3-disubstituted isomer **20** proceeds via a cycloreversion–cycloaddition pathway.[18] Rhodium migration from carbon to oxygen followed by reductive elimination produces the observed furan. This divergent reactivity may be accounted for by the fact that the formal increase in oxidation state (i.e., Rh(I) → Rh(III)) which accompanies the conversion of **18** → **19** is a much more facile process than the comparable Rh(II) → Rh(IV) formal oxidation.[1] A closely related mechanism was suggested by Liebeskind and Cho[19] in their studies of the Rh(I)-catalyzed carbonylation reaction of cyclopropenyl-substituted ketones to α-pyrones. At the present time, however, other possibilities including a regioselective σ-bond oxidative–addition process cannot be unequivocally eliminated.[20,21] Mechanistic studies as well as the synthetic exploration of the reaction is under active investigation.

Scheme II



Acknowledgment. We wish to thank the National Science Foundation for generous support of this work. We also thank Professor Lanny Liebeskind for helpful comments.

Supplementary Material Available: Spectroscopic data for new compounds (4 pages). Ordering information is given on any current masthead page.

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(14) Compound **11**: NMR ($CDCl_3$, 300 MHz) δ 0.96 (t, 3 H, J = 7.5 Hz), 1.62 (m, 2 H), 2.42 (t, 2 H, J = 7.5 Hz), 6.54 (s, 1 H), 7.20–7.23 (m, 1 H), 7.25 (s, 1 H), 7.30–7.36 (m, 2 H), 7.60–7.70 (m, 2 H). Compound **12**: NMR ($CDCl_3$, 300 MHz) δ 0.97 (t, 3 H, J = 7.5 Hz), 1.70 (m, 2 H), 2.63 (t, 2 H, J = 7.5 Hz), 6.03 (d, 1 H, J = 3.0 Hz), 6.51 (d, 1 H, J = 3.0 Hz) 7.17–7.62 (m, 5 H).

(15) Davies, H. M. L.; Clark, D. M.; Alligood, D. B.; Eiband, G. R. *Tetrahedron* **1987**, 4265.

(16) More than likely, the formation of furan **11** proceeds by equilibration of the *Z* → *E* vinyl carbenoid, in analogy to the equilibration observed in related thermal and photochemical cyclopropene–vinylcarbene reactions.[17]

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(18) The ring opening of metallocyclobutenes is well precedented, see: Tebbe, F. N.; Harlow, R. L. *J. Am. Chem. Soc.* **1980**, *102*, 6151. Work is currently in progress to test for exchange of the alkyne in the cage structure with an added 1-alkyne.

(19) Cho, S. K.; Liebeskind, L. S. *J. Org. Chem.* **1987**, *52*, 2633.

(20) An alternate explanation is that Rh(I) activates the carbon–carbon double bond for nucleophilic attack by the carbonyl oxygen. In this sequence, π-coordination by Rh(I) makes the double bond susceptible to nucleophilic attack which occurs at the more substituted carbon. This attack sets in motion the electron rearrangement that results in the observed products. The π-activation mechanism is consistent with the known ability of Rh(I) to cause rearrangements of vinylcyclopropanes; see: Salomon, R. G.; Salomon, M. F.; Kachinski, J. L. C. *J. Am. Chem. Soc.* **1977**, *99*, 1043. Sarel, S. *Acc. Chem. Res.* **1978**, *11*, 204.

(21) Acetylenic α-diazoketone **22**, when treated with 1-hexyne in the presence of 2 mol % Rh_2OAc_4 gave indenone **23** in high yield. In this case, treatment of **23** with either additional Rh_2OAc_4 or $[ClRh(CO)_2]_2$ gave the same rearranged cyclopentadiene derivative **24** in 92% isolated yield. We are investigating the mechanistic details of this reaction using other transition metal catalysts and will report our findings in due course.