transition states for these processes in COT.[14]

Acknowledgment. We thank the National Science Foundation for support of this research and for a grant that allowed purchase of the Convex C-210 Computer, on which some of these calculations were performed. We also thank the San Diego Supercomputer Center for a generous allocation of computer time.

Supplementary Material Available: Optimized CASSCF/3-21G geometries for D_{2d} and D_{4h} COT and optimized CASSCF/3-21G and 6-31G* geometries for D_{8h} (1 page). Ordering information is given on any current masthead page.

---

(14) Our calculations do not, of course, exclude the possibility of nonplanar transition state geometries in annulated derivatives of COT.[5]

A New Phenol Synthesis from the Rhodium(I)-Catalyzed Reaction of Cyclopropenes and Alkynes[†]

Albert Padwa* and Simon L. Xu

Department of Chemistry, Emory University
Atlanta, Georgia 30322

Received March 20, 1992

The Fischer carbene carbonylation reaction represents an important method for the preparation of a variety of substituted phenols.[1-7] This protocol, as illustrated by the assembly in Figure 1, requires a stoichiometric amount of the metal and works best when the carbene complex is stabilized by an oxygen substituent. We recently initiated a study of the rhodium metal mediated cyclizations of acetylenic diazo ketones.[8a] Such substrates are appealing as synthetic intermediates in that they are readily accessible, are reasonably robust, and produce vinyl carbenoids that are useful for further synthetic transformations.[9,10] We have now explored the potential of these rhodium vinyl carbenoid intermediates to undergo alkyne insertion so as to produce substituted phenols. This approach to phenols nicely complements the more traditional benzannulation reaction of Fischer carbene complexes (i.e., **2** vs **5**).

The precursors for the rhodium vinyl carbenoids were prepared in good yields by treating α-diazo benzoyl ketone with various terminal alkynes.[11] The resulting cyclopropene **6** was allowed to stir in methylene chloride with 10 mol % of tetracarbonyldichlorodirhodium in the presence of another terminal alkyne. In a typical reaction, cyclopropene **6a** was reacted with 1-hexyne to give oxepin **7a** (62%) as well as phenol **8a** (8%). A related set of reactions occurred with methyl propargyl ether (**7b** (54%) and **8b** (7%)) as well as with 4-phenyl-1-butyne (**7c** (45%)). The NMR spectrum of oxepin **7a** shows a vinyl singlet at δ 5.45 and two sets of vinylic doublets at 6.05 and 6.27 with a vicinal coupling constant of 6.1 Hz. Treatment of oxepin **7** with a drop of HCl at 40 °C induced a near-quantitative rearrangement to phenol **9**.[12]

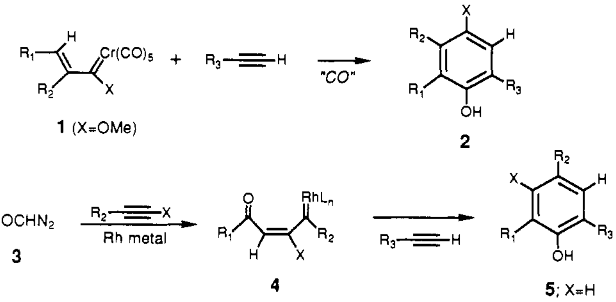
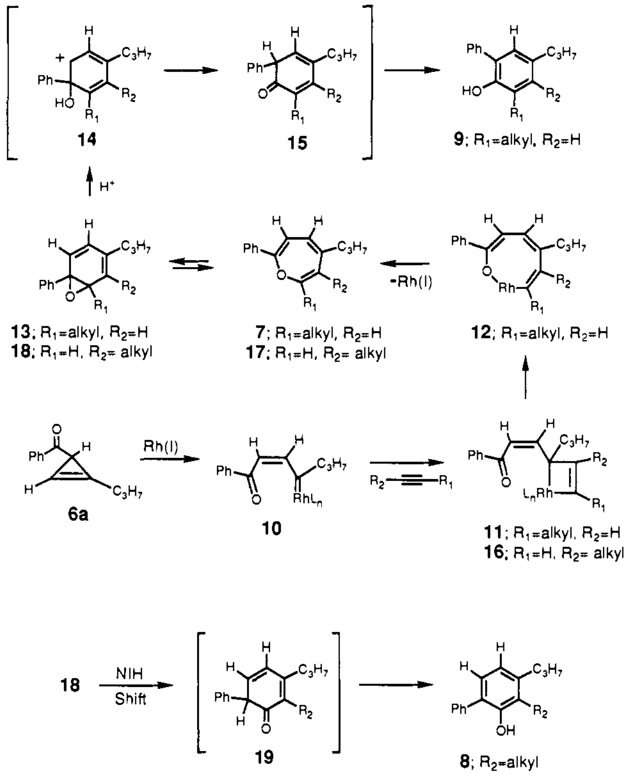
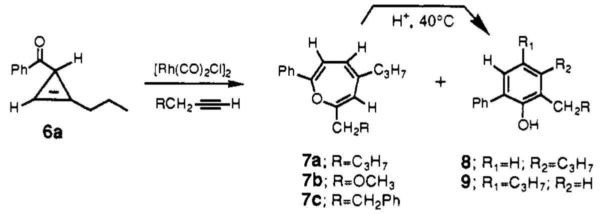


Figure 1. Fischer carbene vs rhodium carbenoid approach to substituted phenols.

Scheme I





[†] Dedicated to my good friend Al Meyers on the occasion of his 60th birthday.

(1) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 644.

(2) For a review, see: Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1990; Vol. 5. Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press, Inc.: Greenwich, CT, 1989; Vol. 1. McCallum, J. S.; Kunng, F.-A.; Gilbertson, S. R.; Wulff, W. D. *Organometallics* **1988**, *7*, 2346. Wulff, W. D.; Xu, Y.-C. *Tetrahedron Lett.* **1988**, 415.

(3) Boger, D. L.; Jacobson, I. C. *J. Org. Chem.* **1990**, *55*, 1919.

(4) Yamashita, A. *J. Am. Chem. Soc.* **1988**, *107*, 5823.

(5) Peterson, G. A.; Kunng, F.-A.; McCallum, J. S.; Wulff, W. D. *Tetrahedron Lett.* **1987**, 1381.

(6) Dötz, K. H.; Popall, M. *Tetrahedron* **1985**, *41*, 5797. Dötz, K. H.; Dietz, R. *Chem. Ber.* **1978**, *111*, 2517.

(7) Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E. J.; Wu, W.; Zask, A. *Tetrahedron* **1985**, *41*, 5803.

(8) (a) Padwa, A.; Kassir, J. M.; Xu, S. L. *J. Org. Chem.* **1991**, *56*, 6971. (b) Electrophilic attack of Rh(I) probably occurs initially on the less substituted carbon of the cyclopropene π-bond but the resulting metalated species is equilibrated to the more stable rhodium-carbene complex **10**.[8a,13]

(9) Padwa, A.; Austin, D. J.; Xu, S. L. *J. Org. Chem.* **1992**, *57*, 1330. Padwa, A.; Krumpe, K. E.; Zhi, L. *Tetrahedron Lett.* **1989**, 2623. Padwa, A.; Chiacchio, U.; Gareau, Y.; Kassir, J. M.; Krumpe, K. E.; Schoffstall, A. M. *J. Org. Chem.* **1990**, *55*, 414. Padwa, A.; Krumpe, K. E.; Gareau, Y.; Chiacchio, U. *J. Org. Chem.* **1991**, *56*, 2523. Padwa, A.; Austin, D. J.; Xu, S. L. *Tetrahedron Lett.* **1991**, 4103. Kinder, F. R.; Padwa, A. *Tetrahedron Lett.* **1990**, 6835.

(10) Hoye, T. R.; Dinsmore, C. J.; Johnson, D. S.; Korkowski, P. F. *J. Org. Chem.* **1990**, *55*, 4518. Hoye, T. R.; Dinsmore, C. J. *J. Am. Chem. Soc.* **1991**, *113*, 43. Hoye, T. R.; Dinsmore, C. J. *Tetrahedron Lett.* **1991**, 3755.

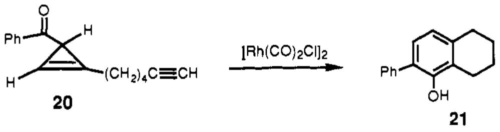
(11) Müller, P.; Pautex, N.; Doyle, M. P.; Bagheri, V. *Helv. Chim. Acta* **1991**, *73*, 1233.

(12) The NMR spectrum of **9** showed the aromatic protons to be coupled by 1.5 Hz (meta). In contrast, phenol **8** exhibited a vicinal coupling of 7.5 Hz for the ortho hydrogens.

0002-7863/92/1514-5881$03.00/0

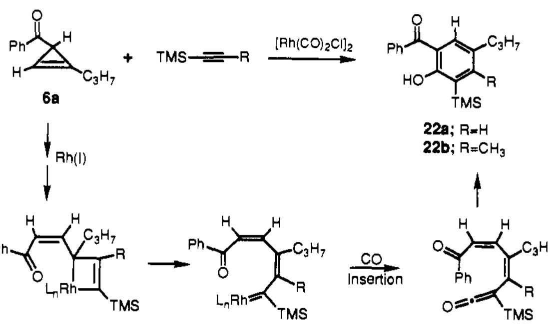
Our mechanistic rationale to account for the Rh(I)-catalyzed transformation is shown in Scheme I. Electrophilic attack of $[ClRh(CO)_2]_2$ on the more substituted carbon of the cyclopropene π-bond[8b] is followed by ring opening to give the rhodium–carbene complex **10**.[11,13] This carbenoid undergoes a subsequent [2 + 2]-cycloaddition reaction with the terminal alkyne in a manner analogous to that encountered with its Fischer carbene counterpart. Two cycloaddition pathways are possible. The major route is favored due to a minimization of steric interactions between the alkyl group on the carbenoid center and the substituent on the alkyne carbon. The resulting rhodacycle **11** rearranges to **12** either by a direct 1,5-sigmatropic shift or via a sequence involving a retro [2 + 2] ring opening followed by an 8π electrocyclization. The transient species **12** undergoes reductive elimination of rhodium to produce the observed oxepin **7**. A related sequence of reactions nicely rationalizes the formation of the minor phenol **8**, which is derived by an NIH shift[14] of the nonisolable oxepin **17** (i.e., **17** → **18** → **19** → **8**). Apparently, the presence of substituent groups on the 2- and 7-positions of oxepin **7** enhances its stability, thereby allowing for its isolation and characterization.[15] Oxepin **7** is in ready equilibrium with arene oxide **13**, and this transient undergoes a 1,2-phenyl shift upon treatment with acid to produce phenol **9** (via **15**) in excellent yield.[16]

Encouraged by the bimolecular trapping results, we decided to investigate the intramolecular annulation reaction of cyclopropene **20** with the Rh(I) catalyst. The annulated phenol **21** was isolated in 45% yield and is presumably formed by a mechanism related to that described in Scheme I.



The above phenol synthesis has several attractive features worth noting. Mechanistically, cycloaddition of the carbenoid with a terminal alkyne (**10** → **11**) is a highly selective process which proceeds in a manner similar to that involved in the Fischer carbene benzannulation process. Instead of introducing the "CO" by insertion, the CO unit is already built into the backbone and is well set up for cyclization to the oxepin ring. The readily available acylcyclopropene ring serves as a 4-carbon synthon. Easy access to a variety of α-diazo ketones and terminal alkynes provides additional leverage to introduce a diverse array of substituents onto the phenol backbone. Finally, rather than using stoichiometric amounts of metal, an efficient catalytic cycle is involved.

One final point has to do with the reaction of cyclopropene **6** with trimethylsilyl-substituted alkynes. Introduction of the silyl group on the alkyne caused a significant change in the character of the reaction. Thus, when cyclopropene **6** was treated with (trimethylsilyl)acetylene in the presence of $[Rh(CO)_2Cl]_2$, none of the expected product was observed. Instead, a low yield of phenol **22a** was isolated. Carrying out the reaction under a CO atmosphere, however, afforded phenol **22a** in 47% yield. A related reaction also occurred using (trimethylsilyl)-1-propyne (i.e., **22b**). We suspect that the reaction proceeds via rhodacycle **23**, which ring opens to give **24**. This transient species prefers to undergo CO insertion, and this is followed by 6π electrocyclization and tautomerization to produce **22**.[17] The dramatic difference which results from changing the alkyne substituent to a silyl group is not totally understood. Perhaps the steric bulk of the trimethylsilyl group present in **24** prevents this transient from achieving the proper geometry necessary for cyclization to the 8-membered rhodacycle. Alternatively, the ability of a silicon atom to stabilize the ketene backbone may promote the insertion reaction.[18] It should be noted that the CO insertion encountered here is significantly different from that reported by Liebeskind and Cho which provided α-pyrones.[13]



In conclusion, we have demonstrated that the Rh(I)-catalyzed reaction of acylcyclopropenes represents a new and novel approach toward substituted phenols. Further studies on the mechanism and synthetic potential of this method are in progress.

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

Supplementary Material Available: Listing of spectroscopic data for new compounds (5 pages). Ordering information is given on any current masthead page.

---

[13] Cho, S. H.; Liebeskind, L. S. *J. Org. Chem.* **1987**, *52*, 2631.

[14] Daly, J. W.; Jerina, D. M.; Witkop, B. *Experientia* **1972**, *28*, 1129.

[15] Boyd, D. R. *Chem. Heterocycl. Compd.* **1985**, *42*, 197.

[16] The formation of phenol **9** from oxepin **13** seemingly involves an acid-catalyzed opening of the epoxide ring to give the less stable carbocation. More than likely, the conversion of **13** to the other isomeric dienyl cation is reversible and the facility of phenyl migration (vs alkyl) accounts for the preferential formation of phenol **9**.

[17] Vinylketenes bearing unsaturated substituents at C-4 are known to cyclize to phenols; see: Danheiser, R. L.; Brisbois, R. G.; Kowalczyk, J. J.; Miller, R. F. *J. Am. Chem. Soc.* **1990**, *112*, 3093. Krysan, D. K.; Gurski, A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1992**, *114*, 1412. Perri, S. T.; Moore, H. W. *J. Am. Chem. Soc.* **1990**, *113*, 1897.

[18] Allen, A. D.; Tidwell, T. T. *Tetrahedron Lett.* **1991**, 847 and references cited therein.

Very Fast Ester Hydrolysis by a Cyclodextrin Dimer with a Catalytic Linking Group

Ronald Breslow* and Biliang Zhang

Department of Chemistry, Columbia University
New York, New York 10027

Received April 20, 1992

Many artificial enzymes have been constructed with catalytic groups added to substrate binders such as cyclodextrins or synthetic cavities.[1] However, multiple binding interactions are needed to fix the geometry of a reactive substrate center relative to the catalytic groups. This approach was employed in the remote functionalizations of flexible substrates.[2,3]

Very high binding constants can result when two cyclodextrins are linked in ditopic hosts for substrates that have two hydrophobic ends,[4] particularly if *two* linking chains are used.[5] We have now prepared a cyclodextrin dimer with a metal-binding group in the linker. With substrate esters that doubly bind so as to put the ester group next to the metal ion, catalytic hydrolysis occurs with good turnover and very high rate accelerations. The mechanism apparently involves attack by a metal hydroxide species, as in many metalloenzymes.

---

[1] For a recent review with references, cf. Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 317–324.

[2] Breslow, R.; Rajagopalan, R.; Schwarz, J. *J. Am. Chem. Soc.* **1981**, *193*, 2905–2906.

[3] Breslow, R.; Brown, A. B.; McCullough, R. D.; White, P. W. *J. Am. Chem. Soc.* **1989**, *111*, 4517–4518.

[4] Breslow, R.; Greenspoon, N.; Guo, T.; Zarzycki, R. *J. Am. Chem. Soc.* **1989**, *111*, 8296–8297.

[5] Breslow, R.; Chung, S. *J. Am. Chem. Soc.* **1990**, *112*, 9659–9660.

0002-7863/92/1514-5882$03.00/0