Ruthenium-Catalyzed Addition of Alkenes to Acetylenes

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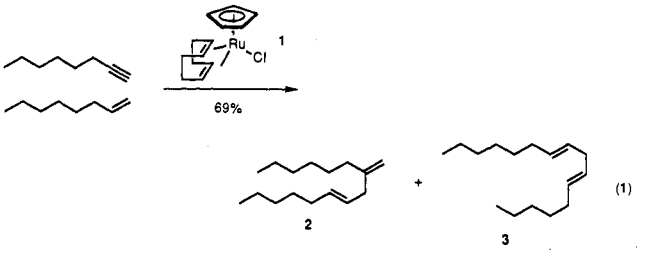
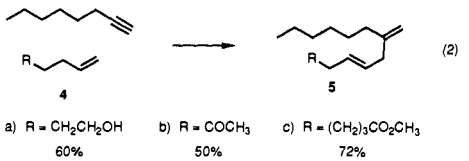
Synthetic efficiency requires reactions that are both selective and atom economical.[1] Reactions that maximize the latter are of the form A + B → C with any other reagents being required only in catalytic amounts. Few of our reactions meet this criterion. Those that do, exemplified by the Diels–Alder reaction, have proven to be extraordinarily important and practical. As part of a program to search for such addition processes, we discovered a remarkably selective ene-type addition of an acetylene with an alkene catalyzed by a ruthenium complex.

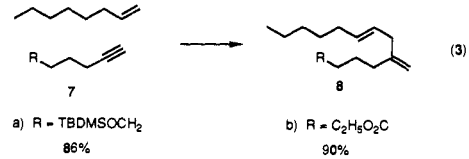
The prospect to promote additions of olefins to acetylenes derived from our observations of olefin migration via C–H insertion with ruthenium complexes and the importance that ligands on ruthenium had on the selectivity.[2] The key becomes finding a complex with multiple highly labile ligands but with the capability of maintaining its catalytic activity. This concept led to the exploitation of Cp(COD)RuCl (**1**).[2,3] Heating a 1:1 mixture of 1-octene and 1-octyne in 3:1 DMF–water at 100 °C with 5 mol % of ruthenium complex **1**[4] for 2 h (eq 1) gave a 1:1 adduct whose



spectroscopic properties clearly showed it to be the branched 1,4-diene **2**[5] with a small amount of the regioisomeric linear adduct **3** also produced (**2**:**3**, 5:1). Using the above protocol, we explored the chemoselectivity by varying the olefin partner to include an unprotected alcohol (**4a**), a ketone (**4b**), and an ester (**4c**). In each of these cases, the reaction proceeded equally well to give the branched products **5a–c**[5] as the major ones (4:1 branched: linear), as depicted in eq 2.

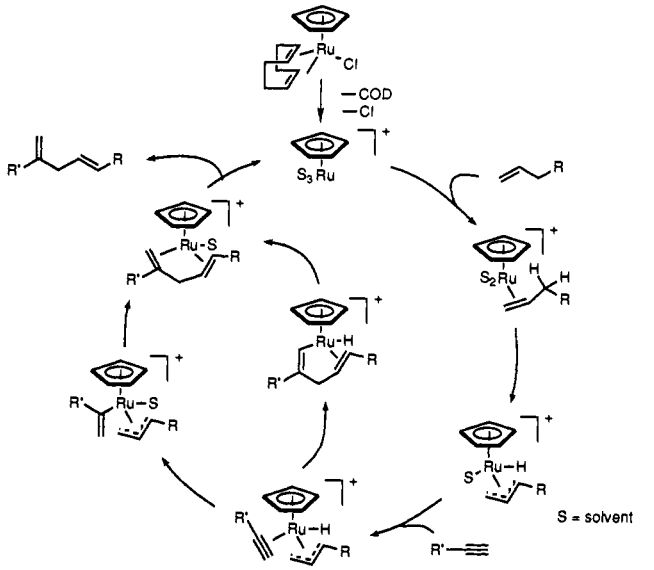


Functional groups in the acetylenic partner did not affect the process, as depicted in eq 3. The reactions gave excellent yields

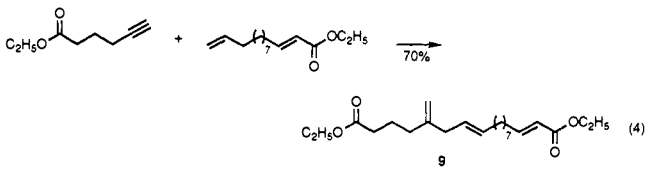


(1) Trost, B. M. *Science* **1991**, *254*, 1471.
(2) Trost, B. M.; Kulawiec, R. J. *Tetrahedron Lett.* **1991**, *32*, 3039; *J. Am. Chem. Soc.* **1993**, *115*, 2027.
(3) Other ruthenium compounds including ruthenium trichloride and benzeneruthenium dichloride fail to effect reaction. Cp* ruthenium dichloride was explored in a related reaction but **1** gives the best selectivity and reactivity.

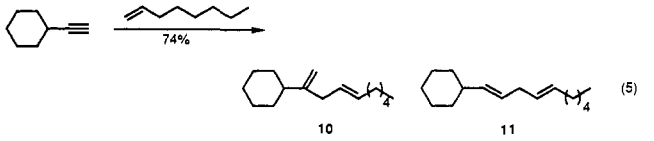
Scheme I. A Mechanistic Rationale



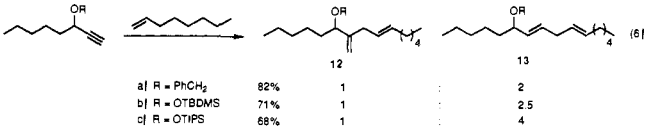
and regioselectivities (branched:linear, 5–6:1) of the 1:1 adducts **8a**[5] and **8b**.[5] A most interesting example of chemoselectivity is the example of eq 4, in which a normally reactive enoate[6] does not interfere.



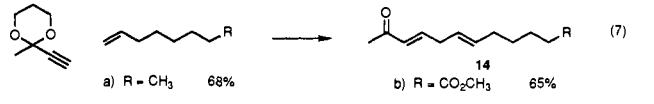
Substituents at the propargylic position of the acetylenic partner had an important effect on the regioselectivity of the addition. Branching at that center as in the case of 1-ethynylcyclohexane diminished the regioselectivity (eq 5, **10**[5]:**11**, 2:1). A propargylic



oxygen substituent inverts the regioselectivity to favor the linear product **13**[5] with the ratio reflecting the size of the oxygen substituent (eq 6). Increasing steric hindrance by placing a ketal



at the propargylic position further increases the selectivity for the linear addition product **14**[5] to 6:1 (eq 7). In these cases, the conjugated ketal hydrolyzed under the reaction conditions. The observed 15–16-Hz coupling constants for both olefinic linkages indicate the (*E*,*E*)-geometry.



Disubstituted acetylenes also participate in this addition reaction. With a symmetrical internal acetylene as a substrate,

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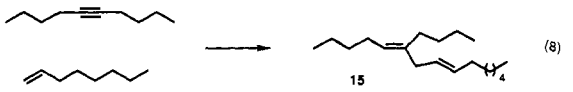
only one regioisomeric product with respect to the acetylene, i.e., **15**,[5] is possible (eq 8).



The success of this new addition reaction is quite remarkable considering all of the potential complications. Why is an allylic position activated for substitution over a propargylic or the terminal acetylenic carbon?[7] Why does cross-addition occur rather than homoaddition? What influences regioselectivity with respect to both reaction partners? While both regioisomers with respect to the acetylene may be seen, only one regioisomer with respect to the olefin is observed. Scheme I presents a rationale which can address these questions which, because of space limitations, is presented without comment.[8] Further studies to probe these questions and to explore the many exciting facets of this new carbon–carbon bond-forming process are underway.

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Supplementary Material Available: Experimental procedures and characterization data for **2**, **5**, and **8**–**15** (5 pages). Ordering information is given on any current masthead page.

(4) Albers, M. O.; Robinson, D. J.; Shaver, A.; Singleton, E. *Organometallics* **1986**, *5*, 2199.

(5) This compound has been satisfactorily characterized spectroscopically.

(6) Cf. Mitsudo, T.; Zhang, S.; Nagao, M.; Watanabe, Y. *Chem. Commun.* **1991**, 599.

(7) Cf. Mitsudo, T.; Hori, Y.; Watanabe, Y. *J. Organomet. Chem.* **1987**, *334*, 157. Dahlenberg, L.; Frosin, K. M.; Kerstan, S.; Werner, D. B. *J. Organomet. Chem.* **1991**, *407*, 115. Echavarren, A. M.; Lopez, J.; Santos, A.; Montoya, J. *J. Organomet. Chem.* **1991**, *414*, 393.

(8) A reaction involving a ruthenacyclopentene intermediate may also be envisioned, see ref 5. The absence of homocoupled products, the nonreactivity of acetylenes in the absence of olefins, and the propensity for olefin isomerization in the absence of acetylenes leads us to favor the rationale presented in the scheme at present. We observe that COD is removed from the ruthenium by reaction with the acetylene to give a 1:1 adduct, a reaction currently under investigation.