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Mechanism of Molybdenum Pentacarbonyl-Catalyzed Cyclizations of Alkynols and Epoxyalkynes

Frank E. McDonald*[1a] and Colleen C. Schultz[1b]

Department of Chemistry, Northwestern University
2145 Sheridan Road, Evanston, Illinois 60208-3113

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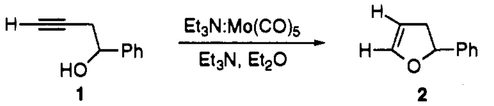
We recently reported that molybdenum pentacarbonyl will cyclize 1-alkyn-4-ols to the isomeric 2,3-dihydrofurans.[2,3] Although the generation of $\mathrm{Mo(CO)_5}$ from trimethylamine *N*-oxide and molybdenum hexacarbonyl produces a modestly catalytic reagent for this cycloisomerization, we have found that $\mathrm{Et_3N{:}Mo(CO)_5}$ is best prepared by photolysis of $\mathrm{Mo(CO)_6}$ in a mixture of diethyl ether and triethylamine (Rayonet lamp, 350 nm, pyrex filter, eq 1).[4] Subsequent addition of alkynol **1**[5] (dark reaction)

$$\mathrm{Mo(CO)_6} \xrightarrow[\mathrm{Et_3N,\ Et_2O}]{h\nu\ \text{(Pyrex filter)},} \mathrm{Et_3N{:}Mo(CO)_5} \qquad (1)$$



(2)

and stirring for ca. 18 h gives dihydrofuran **2**[6] (89% optimized yield from 26 mol % $\mathrm{Mo(CO)_6}$, eq 2). This reaction system is critically dependent on the presence of a tertiary amine, in that photogenerated molybdenum pentacarbonyl–diethyl ether leaves **1** unchanged. A practical advantage of supplanting trimethylamine *N*-oxide decarbonylation with the photochemical method is that cyclic products are more effectively removed from inorganic byproducts, thus resulting in higher isolated yields.

Attempts to follow the mechanistic course of this reaction by deuterium-labeling of either the alcohol or alkynyl hydrogens of **1** were complicated by equilibration of the deuterium atom between these two moderately acidic functional groups upon standing in the absence of triethylamine or molybdenum carbonyls.[7] However, our current evidence for the intermediacy of molybdenum carbene anion **4** as a catalytic intermediate includes the isolation of the apparent aldol condensation–dehydration[8] products **5** and **6** (Scheme 1). Reaction of **1** with 1 equiv of $\mathrm{Et_3N{:}Mo(CO)_5}$ in the presence of benzaldehyde gives the stable, blood-red molybdenum carbene **5** (35% yield) along with dihydrofuran **2** (37%), while the catalytic reaction with enolizable acetaldehyde[9] gives the conjugated diene **6** as an inseparable mixture with **2**.

Scheme 1. Proposed Mechanism for Alkynol Cycloisomerization

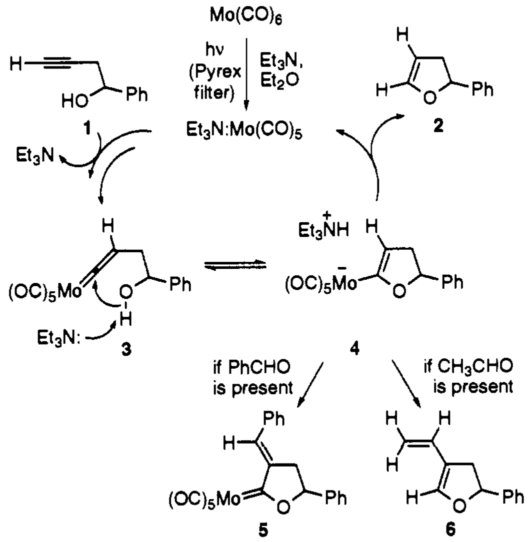
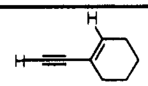
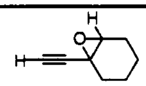
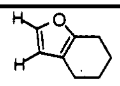
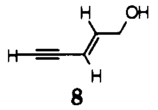
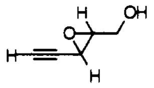
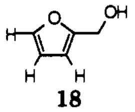
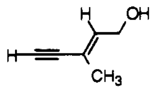
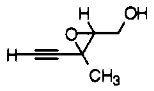
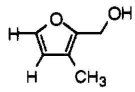
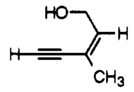
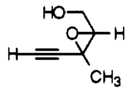
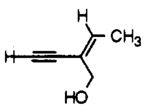
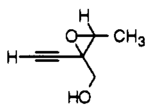
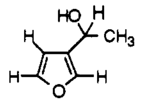


Table 1. Cycloisomerization of Epoxyalkynes to Furans[a]

entry	enyne	epoxyalkyne	furan	furan yield
1	 **7**	 **12**	 **17**	85%
2	 **8**	 **13**	 **18**	76%
3	 **9**	 **14**	 **19**	83%
4	 **10**	 **15**	**19**	85%
5	 **11**	 **16**	 **20**	63%

[a] Representative procedure: $\mathrm{Mo(CO)_6}$ (0.3 mmol) was placed in an 18- × 150-mm borosilicate test tube. Freshly distilled $\mathrm{Et_3N}$ (3 mL) and $\mathrm{Et_2O}$ (10 mL) were added, and the contents were dissolved with stirring. The reaction mixture was then photolyzed for 20 min under $\mathrm{N_2}$. The reaction vessel was removed from the light source, epoxyalkynes **12–16** (2.0 mmol) in $\mathrm{Et_2O}$ (2 mL) were added, the reaction mixture was left to stir for 18 h. Furan products **17–20** were isolated by evaporation of solvent followed by flash chromatography on silica gel (pentane:$\mathrm{Et_2O}$).

We also found that epoxyalkyne **12** (prepared by *m*-CPBA epoxidation[10] of enyne **7**[11]) reacts with a catalytic amount (11

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[1] (a) Camille and Henry Dreyfus New Faculty Awardee, 1992–1997. (b) Formerly published as Colleen B. Connolly.

[2] McDonald, F. E.; Connolly, C. B.; Gleason, M. M.; Towne, T. B.; Treiber, K. D. *J. Org. Chem.* **1993**, *58*, 6952.

[3] Other middle and late transition metal complexes react with terminal alkynols to give cyclic oxacarbenes. (a) Quayle, P.; Rahman, S.; Ward, E. L. M.; Herbert, J. *Tetrahedron Lett.* **1994**, *35*, 3801. (b) Hinkle, R. J.; Stang, P. J.; Arif, A. M. *Organometallics* **1993**, *12*, 3510. (c) Stang, P. J.; Huang, Y. H. *J. Organomet. Chem.* **1992**, *431*, 247. (d) Le Bozec, H.; Ouzzine, K.; Dixneuf, P. H. *Organometallics* **1991**, *10*, 2768. (e) O'Connor, J. M.; Pu, L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1990**, *112*, 6232. (f) Dötz, K. H.; Sturm, W.; Alt, H. G. *Organometallics* **1987**, *6*, 1424. (g) Parlier, A.; Rudler, H. *J. Chem. Soc., Chem. Commun.* **1986**, 514. (h) Curtis, P. J.; Davies, S. G. *J. Chem. Soc., Chem. Commun.* **1984**, 747. (i) Marten, D. F. *J. Chem. Soc., Chem. Commun.* **1980**, 341. (j) Bruce, M. I.; Swincer, A. G.; Thomson, B. J.; Wallis, R. C. *Aust. J. Chem.* **1980**, *33*, 2605. (k) Oguro, K.; Wada, M.; Okawara, R. *J. Organomet. Chem.* **1978**, *159*, 417. (l) Clark, H. C.; Manzer, L. E. *J. Organomet. Chem.* **1973**, *47*, C17. (m) Chisholm, M. H.; Clark, H. C. *J. Am. Chem. Soc.* **1972**, *94*, 1532.

[4] (a) Wrighton, M. *Chem. Rev.* **1974**, *74*, 401. (b) Arndt, L. W.; Bischoff, C. J.; Darensbourg, M. Y. *Inorg. Synth.* **1989**, *26*, 335. (c) Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154.

[5] Brandsma, L. *Preparative Acetylenic Chemistry*, 2nd ed.; Elsevier: Amsterdam, 1988; p 67.

[6] Hillers, S.; Niklaus, A.; Reiser, O. *J. Org. Chem.* **1993**, *58*, 3169.

[7] Although alcohols are generally considered to be significantly more acidic than terminal alkynes, Bordwell has shown that in aprotic solvent (DMSO), a representative terminal alkyne (ethynylbenzene, $\mathrm{p}K_a$ 28.7) is slightly more acidic than a secondary alcohol (2-propanol, $\mathrm{p}K_a$ 30.25). Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

[8] (a) Casey, C. P.; Brunsvold, W. R. *J. Organomet. Chem.* **1975**, *102*, 175. (b) Wulff, W. D.; Anderson, B. A.; Toole, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 5485.

[9] Lattuada, L.; Licandro, E.; Maiorana, S.; Papagni, A. *J. Chem. Soc., Chem. Commun.* **1991**, 437.

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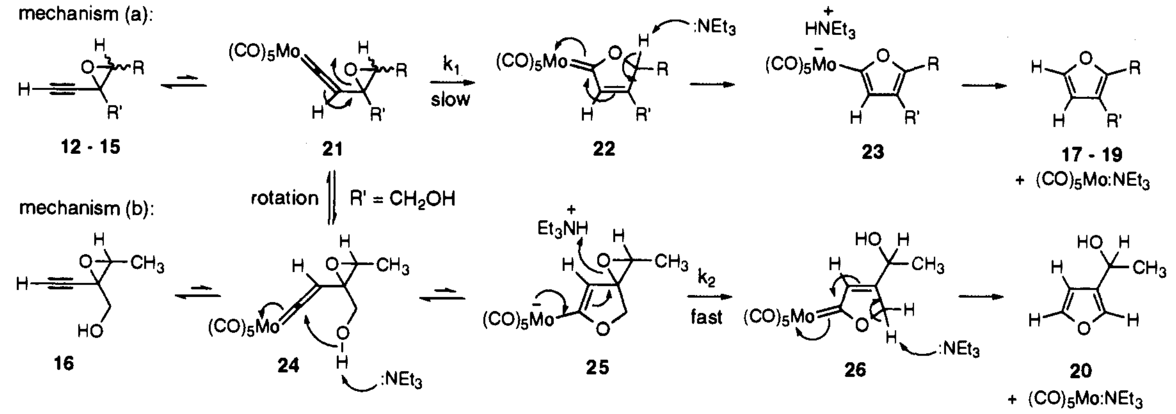
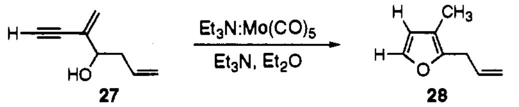
Scheme 2. Proposed Mechanisms for Cycloisomerization of Epoxyalkynes **12–16**



mol %) of triethylamine–molybdenum pentacarbonyl to give the furan product **17**[12,13] in good yield (entry 1, Table 1). Our selection of subsequent epoxyalkyne substrates **13–16**[10,11] was designed in part to test various mechanistic issues. For example, the mechanistic possibility of base-induced elimination of the epoxide to an alkynyl allylic alcohol intermediate[13e] is precluded in substrate **13**, which provides furfuryl alcohol **18** (entry 2) under the same reaction conditions used to convert epoxyalkyne **14** to furan **19** (entry 3). For compound **15**[14] (entry 4), which has the alcohol and alkynyl groups *cis*-substituted on the oxirane ring, the only product observed is **19**.[15] However, when the hydroxyl group is placed in a homopropargylic position (**16**, entry 5), we observe only the product **20**,[16] in which the furan oxygen arises from the alcohol, while the exocyclic secondary alcohol results from epoxide opening.

We propose that the $Et_3N{:}Mo(CO)_5$-catalyzed isomerization to furans generally proceeds by way of a concerted rearrangement[17,18] of epoxyvinylidenecarbenes **21** to the cyclic α,β-alkenyloxacarbene intermediate **22** (mechanism a, Scheme 2). Vinylogous deprotonation of **22** and subsequent protonation[19] of the molybdenum–furan bond of **23** (possibly by reductive elimination of a furylmolybdenum hydride) will yield furans **17–19**. In the case of hydroxylated epoxyalkyne **16** (entry 5, Table 1), the vinylidenecarbene **24** is rapidly trapped by the pendant hydroxyl group to give anionic **25**. The equilibrium between **24** and **25** is presumably driven by epoxide opening to the cyclic α,β-alkenyloxacarbene intermediate **26** (mechanism b). The divergence between mechanisms a and b is probably due to the relative differences in the irreversible rate-determining steps, where $k_1 < k_2$, and so mechanism b dominates mechanism a when a homopropargylic alcohol is present to trap the vinylidenecarbene intermediate before it can rearrange to cyclic α,β-alkenyloxacarbene. We have observed that primary homopropargylic alcohols such as 3-butyn-1-ol and enynol **11** are generally unreactive under $Et_3N{:}Mo(CO)_5$ catalysis, but the relief of strain energy gained by epoxide opening (**25** → **26**) drives this otherwise unfavorable example to the furan **20**.

We have also found that the secondary hydroxyenyne **27**[20] will cyclize to give the furan product **28** (64% yield, eq 3) as a result of migration of the *exo*-methylene to give the aromatic furan.



(3)

Note that the allyl side chain does not migrate into conjugation with the furan ring under these mild reaction conditions. Further studies on the scope of molybdenum pentacarbonyl-catalyzed cyclizations are in progress.

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Supplementary Material Available: Tabulated spectral data for compounds **5**, **19**, **27**, and **28** (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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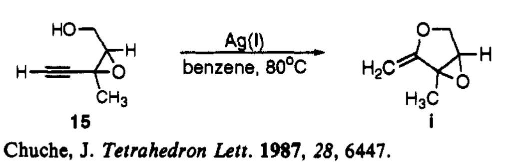
(10) (a) Carlson, R. G.; Cox, W. W. *J. Org. Chem.* **1977**, *42*, 2382. (b) Schmidt, U.; Respondek, M.; Leiberknect, A.; Werner, J.; Fischer, P. *Synthesis* **1989**, 256.

(11) Enynes **7–10** are commercially available. Compound **11** was prepared in four steps from 2-buten-1-ol: (1) Br_2, $CHCl_3$; (2) powdered KOH, Et_2O (21%, two steps); (3) (trimethylsilyl)acetylene, 5% $Pd(PPh_3)_2Cl_2$, CuI, Et_2NH (58%); (4) 50% aqueous KOH, $BnEt_3NCl$, CH_2Cl_2 (94%).

(12) Scharf, H. D.; Walters, E. *Chem. Ber.* **1978**, *111*, 639.

(13) Several methods have recently been developed for furan synthesis: (a) Trost, B. M.; Flygare, J. A. *J. Org. Chem.* **1994**, *59*, 1078. (b) Katritzky, A. R.; Li, J.; Gordeev, M. F. *J. Org. Chem.* **1993**, *58*, 3038. (c) Tani, K.; Sato, Y.; Okamoto, S.; Sato, F. *Tetrahedron Lett.* **1993**, *34*, 4975. (d) Arcadi, A.; Cacchi, S.; Larock, R. C.; Marinelli, F. *Tetrahedron Lett.* **1993**, *34*, 2813. (e) Marshall, J. A.; DuBay, W. J. *J. Am. Chem. Soc.* **1992**, *114*, 1450. (f) Fukuda, Y.; Shiragami, H.; Utimoto, K.; Nozaki, H. *J. Org. Chem.* **1991**, *56*, 5816. (g) Takai, K.; Tezuka, M.; Kataoka, Y.; Utimoto, K. *J. Org. Chem.* **1990**, *55*, 5310.

(14) In contrast, Lewis acid-catalyzed cyclization of **15** gives the isomeric exocyclic enol either **i** resulting from addition to the internal carbon of the alkyne.



Pale, P.; Chuche, J. *Tetrahedron Lett.* **1987**, *28*, 6447.

(15) Leonardi, A.; Cazzulani, P.; Nardi, D. *Boll. Chim. Farm.* **1982**, *121*, 1.

(16) Kitamura, T.; Kawakami, Y.; Imagawa, T.; Kawanisi, M. *Synth. Commun.* **1977**, *7*, 521.

(17) Thermal rearrangements of vinyloxiranes to dihydrofurans are known; however, most known cases proceed by carbon–carbon bond-breaking.[18] Carbon–oxygen bond cleavage (analogous to **21** → **22**) requires electron-donating groups (ether, thioether substituents) at the distal terminus of the alkene. (a) Garst, M. E.; Spencer, T. A. *J. Am. Chem. Soc.* **1973**, *95*, 250. (b) Harris, C. M.; Cleary, J. J.; Harris, T. M. *J. Org. Chem.* **1974**, *39*, 72. (c) Okazaki, R.; Negishi, Y.; Inamoto, N. *J. Org. Chem.* **1984**, *49*, 3819.

(18) (a) For a recent review, see: Hudlicky, T.; Reed, J. W. *Comprehensive Organic Synthesis: Selectivity, Strategy, and Efficiency in Modern Organic Chemistry*; Pergamon Press: New York, 1991; Vol. 5, Chapter 8.1, pp 899–970. (b) Hudlicky, T.; Barbieri, G. *J. Org. Chem.* **1991**, *56*, 4598.

(19) (a) Fischer, E. O.; Plabst, D. *Chem. Ber.* **1973**, *107*, 3326. (b) Casey, C. P.; Brunsvold, W. R. *Inorg. Chem.* **1977**, *16*, 391. (c) Soderberg, B. C.; Turbeville, M. J. *Organometallics* **1991**, *10*, 3951. (d) Iwasawa, N.; Saitou, M. *Chem. Lett.* **1994**, 231.

(20) Prepared in three steps from 2-bromoacrolein (Smith, A. B.; Levenberg, P. A.; Jerris, P. L.; Scarborough, R. M.; Wovkulich, P. M. *J. Am. Chem. Soc.* **1981**, *103*, 1501. Della, E. W.; Pigou, P. E. *Aust. J. Chem.* **1983**, *36*, 2261): (1) allylmagnesium bromide, Et_2O (74%); (2) (trimethylsilyl)acetylene, 5% $Pd(PPh_3)_2Cl_2$, CuI, Et_2NH (37%); (3) 50% aqueous KOH, $BnEt_3NCl$, CH_2Cl_2 (69%).