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

Received June 24, 1994

We recently reported that molybdenum pentacarbonyl will cyclize 1-alkyn-4-ols to the isomeric 2,3-dihydrofurans.^{2,3} Although the generation of $Mo(CO)_5$ from trimethylamine *N*-oxide and molybdenum hexacarbonyl produces a modestly catalytic reagent for this cycloisomerization, we have found that Et₃N: $Mo(CO)_5$ is best prepared by photolysis of $Mo(CO)_6$ in a mixture of diethyl ether and triethylamine (Rayonet lamp, 350 nm, pyrex filter, eq 1).⁴ Subsequent addition of alkynol 1⁵ (dark reaction)



and stirring for ca. 18 h gives dihydrofuran 2^6 (89% optimized yield from 26 mol % 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 trimethyl-amine *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-dehydration⁸ products 5 and 6 (Scheme 1). Reaction of 1 with 1 equiv of

(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, 6322. (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. 1986, 747. (i) Marten, D. F. J. Chem. Soc., Chem. Commun. 1980, 33, 2605. (k) Oguro, K.; Wada, M.; Okawara, R. 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. Soc. 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, pK₂ 28.7) is slightly more acidic than a secondary alcohol (2-propanol, pK₂ 30.25). Bordwell, F. G. Acc. Chem. Res. 1988, 21, 456.
(8) (a) Casey, C. P.; Brunsvold, W. R. J. Organomet. Chem. 1975, 102,

(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.

Scheme 1. Proposed Mechanism for Alkynol Cycloisomerization



Table 1. Cycloisomerization of Epoxyalkynes to Furans^a



^a Representative procedure: Mo(CO)₆ (0.3 mmol) was placed in an 18-×150-mm borosilicate test tube. Freshly distilled Et₃N (3 mL) and Et₂O (10 mL) were added, and the contents were dissolved with stirring. The reaction mixture was then photolyzed for 20 min under N₂. The reaction vessel was removed from the light source, epoxyalkynes 12-16 (2.0 mmol) in Et₂O (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:Et₂O).

Et₃N: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 acetaldehyde⁹ gives the conjugated diene 6 as an inseparable mixture with 2.

We also found that epoxyalkyne 12 (prepared by m-CPBA epoxidation¹⁰ of enyne 7¹¹) reacts with a catalytic amount (11

(9) Lattuada, L.; Licandro, E.; Maiorana, S.; Papagni, A. J. Chem. Soc., Chem. Commun. 1991, 437.

© 1994 American Chemical Society





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 Et₃N: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).

(11) Enynes 7-10 are commercially available. Compound 11 was prepared in four steps from 2-buten-1-ol: (1) Br₂, CHCl₃; (2) powdered KOH, Et₂O (21%, two steps); (3) (trimethylsilyl)acetylene, 5% Pd(PPh₃)₂Cl₂, CuI, Et₂-NH (58%); (4) 50% aqueous KOH, BnEt₃NCl, CH₂Cl₂ (94%). (12) Scharf, H. D.; Walters, E. Chem. Ber. 1978, 111, 639.

 (12) Schait, H. D., watters, E. Chem. Ber. 1978, 711, 635.
 (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. 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 $21 \rightarrow 22$) requires electrondonating groups (ether, thioether substituents) at the distal terminus of the

donating groups (ether, indefiner 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 81, pp 899–970.
(b) Hudliky, T.; Parkieri, G. J. Org. Chem. 1991, 56, 4508 970. (b) Hudlicky, T.; Barbieri, G. J. Org. Chem. 1991, 56, 4598.

Vinylogous deprotonation of 22 and subsequent protonation¹⁹ 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 Et₃N:Mo(CO)₅ catalysis, but the relief of strain energy gained by epoxide opening $(25 \rightarrow 26)$ drives this otherwise unfavorable example to the furan 20.

We have also found that the secondary hydroxyenyne 27²⁰ 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.



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.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. We also gratefully acknowledge financial support provided by Northwestern University and the Camille and Henry Dreyfus Foundation New Faculty Awards Program.

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.

^{(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.

^{(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) allyimagnesium bromide, Et.O (74%); (2) (trimethylsilyl)acetylene, 5% Pd(PPh₃)₂Cl₂, CuI, Et₂NH (37%); (3) 50% aqueous KOH, BnEt₃NCl, CH₂-Cl₂ (69%).