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These and other questions regarding this unusual pathway[18] are currently under investigation.

Acknowledgment. Dr. David Martin and Shirley Gerpheide of The Upjohn Co. are thanked for providing samples of acivicin and 4-hydroxyacivicin, slants of *Streptomyces sviceus*, and the design of the baffled flask used in fermentations. P. C. Prabhakaran and Rodger Kohnert are thanked for obtaining the ^2H NMR spectra. The work was supported by a grant from the Public Health Service GM 32110 to S.J.G. NMR spectra were obtained on a Bruker AM 400 spectrometer purchased in part by grants from the National Science Foundation (CHE-8216190) and from the M. J. Murdock Charitable Trust to Oregon State University.

Intramolecular $S_{N'}$ Cleavage of Allylic Ethers by Enolate Anions

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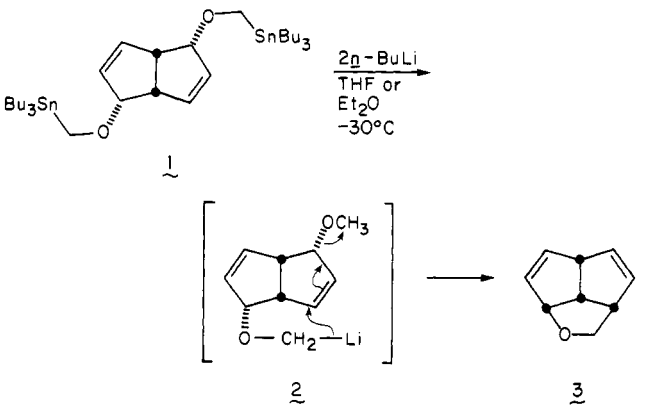
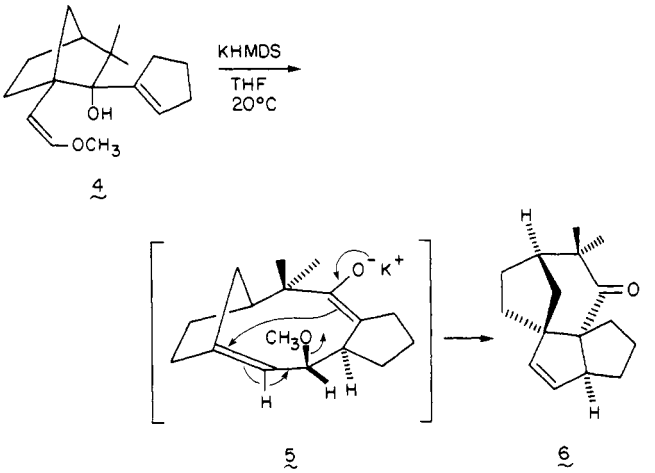
A fundamental property of allylic systems relates to their ability to engage nucleophiles in $S_{N'}$ reaction. Extensive theoretical[2] and experimental investigations[3] over many years attest to the significance attached to the phenomenon. Despite the wide-ranging nature of these studies, however, no attention has been purposefully directed to bimolecular nucleophilic substitution of allyl alkyl ethers, perhaps because of a predetermination that these systems would prove as inert toward displacement as dialkyl ethers. One interesting example known to us is due to Farnum and Monego who showed that dimetalation of **1** proceeds with subsequent proton abstraction from solvent to give **2**, which then experiences intramolecular $S_{N'}$ displacement of methoxide.[4]



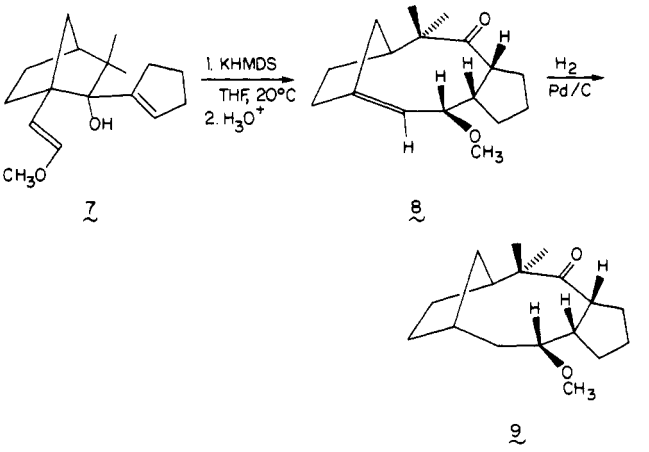
As part of ongoing investigations of anionic oxy-Cope rearrangements,[5,6] our research groups have independently examined the ability of medium-ring enolates to undergo transannular cyclization concomitant with $S_{N'}$ displacement of a methoxyl leaving group. The result is rapid and efficient construction of structurally intricate polycyclic systems.

For example, when alcohol **4**[7] was stirred in anhydrous tetrahydrofuran solution with 1.1 equiv of potassium hexamethyldisilazide at 20 °C for 4 days, smooth conversion to ketone **6** was



observed. Chromatographically purified material, isolated in 51% yield, crystallized as colorless, rectangular plates well suited to X-ray analysis.[8] The suggested pathway to the product diquinane involves initial [3,3]sigmatropic electron reorganization via a chair-like transition state to generate **5**. This process establishes three stereocenters and the double bond geometry. The β-configuration of the methoxyl-substituted carbon results in proper alignment of the C–OCH_3 bond with the flanking π orbital, thereby allowing for the onset of the intramolecular $S_{N'}$ ring closure.

Support for this mechanistic analysis was gained by subjecting **7** to comparable ring expansion. In this instance, **8** was produced efficiently (88%) after only 5.5 h at room temperature. Since crystals of **8** of suitable quality could not be grown, saturation



of its double bond was undertaken. The structure of **9** was subsequently established by crystallographic methods to be as shown.[8] These data indicate the **7** → **8** conversion to be mediated by an

(1) (a) The Ohio State University. (b) Yale University.
(2) (a) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G. *THEOCHEM* **1983**, *12*, 197; *Chem. Abstr.* **1983**, *99*, 211818. (b) Chen, N.; Zhou, B. *Youji Huaxne* **1983**, 257; *Chem. Abstr.* **1983**, *99*, 211825. (c) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 209. (d) Carrion, F.; Dewar, M. J. S. *Ibid.* **1984**, *106*, 3531. (e) Stohrer, W.-D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 613. (f) Houk, K. N. *Pure Appl. Chem.* **1983**, *55*, 277. (g) Murphy, W. S.; O'Mahony, B. *Tetrahedron Lett.* **1981**, *22*, 585.
(3) (a) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901. (b) Overton, K. H. *Chem. Soc. Rev.* **1979**, *8*, 447. (c) Cane, D. E. *Tetrahedron* **1980**, *36*, 1109.
(4) Farnum, D. G.; Monego, T. *Tetrahedron Lett.* **1983**, *24*, 1361.
(5) (a) Schreiber, S. L.; Hawley, R. C. *Tetrahedron Lett.* **1985**, *26*, 5971. (b) Schreiber, S. L.; Santini, C. *J. Am. Chem. Soc.* **1984**, *106*, 4038. (c) Schreiber, S. L.; Santini, C. *Tetrahedron Lett.* **1981**, *22*, 4651.
(6) (a) Paquette, L. A.; Poupart, M.-A. *Tetrahedron Lett.* **1988**, *29*, 273. (b) Paquette, L. A.; DeRussy, D. T.; Rogers, R. D. *Tetrahedron* **1988**, *44*, 3139. (c) Paquette, L. A.; DeRussy, D. T.; Cottrell, C. E. *J. Am. Chem. Soc.* **1988**, *110*, 890. (d) Paquette, L. A.; Learn, K. S.; Romine, J. L.; Lin, H.-S. *Ibid.* **1988**, *110*, 879. (e) Oplinger, J. A.; Paquette, L. A. *Tetrahedron Lett.* **1987**, *28*, 5441. (f) Paquette, L. A.; Pierre, F.; Cottrell, C. E. *J. Am. Chem. Soc.* **1987**, *109*, 5731. (g) Paquette, L. A.; Learn, K. S.; Romine, J. L. *Tetrahedron* **1987**, *43*, 4889. (h) Paquette, L. A.; Romine, J. L.; Lin, H.-S. *Tetrahedron Lett.* **1987**, *28*, 31.
(7) Details relating to the synthesis of this compound will appear elsewhere.
(8) We thank Dr. J. C. Gallucci of the Ohio State University Crystallographic Facility for these analyses.

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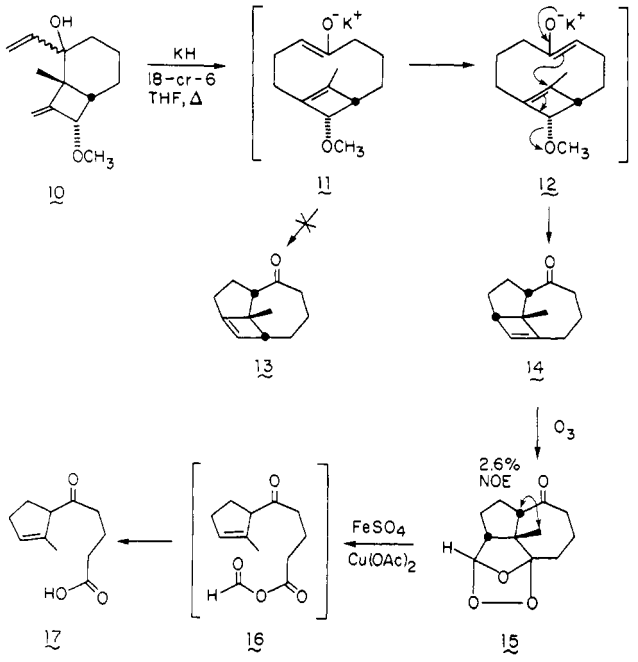
exo-boat transition state.[9] Since the methoxyl substituent in the initially generated enolate anion is consequently α-oriented, i.e., positioned nearly orthogonal to the π electrons, further transannular C–C bond formation is now stereoelectronically disfavored and does not operate.

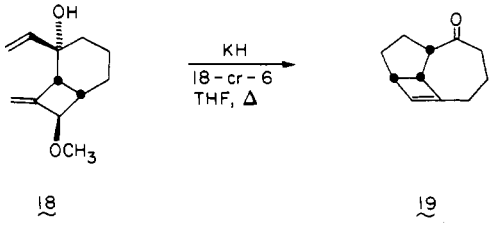
In yet another fascinating reaction, heating of **10** with potassium hydride and 18-crown-6 in dry tetrahydrofuran afforded **14** (40%).



Because detailed spectroscopic analysis of this tricyclic ketone did not allow for definitive determination of the position of its cyclobutene double bond, suitable degradation was undertaken. Thus, ozonolysis of **14** and subsequent treatment of stable ozonide **15** with $FeSO_4/Cu(OAc)_2$[10] in methanol gave the cyclopentene derivative **17**. The formation of **17** unequivocally establishes the site of unsaturation to be as in **14** rather than **13**.

This transformation is believed to originate from enolate anion **11** as the first-formed intermediate. Due to the large amount of strain associated with the bicyclo[3.2.0]hept-1(6)-ene part structure of **13**, intramolecular displacement of methoxide in **11** is energetically disfavored. Instead, enolate isomerization of **11** to **12** operates, with tetrahydrofuran or 18-crown-6 perhaps acting as the proton source, followed by S_N' transannular "scaffolding" to deliver the observed tricyclic product.

In order to scrutinize the kinetic consequences of methoxyl stereochemistry, alcohol **18** was also heated as its potassium salt. Under the same conditions, **19** was isolated in ca. 60% yield.



Charge annihilation within the intermediate enolate anion by S_N' ejection of methoxide must consequently also be facile. This is because modest conformational flexing within cyclobutenes conveniently permits attainment of the necessary stereoalignment from either π face.

Among the many interesting facets of these reactions is their mixed stereochemical course. Whereas the **5** → **6** and **18** → **19** processes involve a trans-antiplanar arrangement of the entering and leaving groups, the conversion of **12** to **14** occurs in syn fashion (as does **2** → **3**). Further, the preceding observations show the S_N' displacement of methoxide by enolate ions to proceed with reasonable efficiency and to constitute an exceptionally powerful synthetic method.

Acknowledgment. This investigation was supported by NIH Grants CA-12115 (to L.A.P.) and GM-32527 (to S.L.S).

(9) The various mechanistic pathways open to these alcohols will be discussed in detail at a later date.

(10) (a) Schreiber, S. L. *J. Am. Chem. Soc.* **1980**, *102*, 6163. (b) Schreiber, S. L.; Liew, W.-F. *Tetrahedron Lett.* **1983**, *24*, 2363. (c) Schreiber, S. L.; Liew, W.-F. *J. Am. Chem. Soc.* **1985**, *107*, 2980. (d) Schreiber, S. L.; Sammakia, T.; Hulin, B.; Schulte, G. *Ibid.* **1986**, *108*, 2106. (e) Schreiber, S. L.; Hulin, B.; Liew, W.-F. *Tetrahedron* **1986**, *42*, 2945.

An Efficient Silylformylation of Alkynes Catalyzed by $Rh_4(CO)_{12}$

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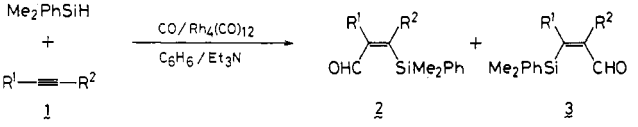
A combination of transition-metal complexes and hydrosilanes is a useful tool for highly selective transformations of alkenes, alkynes, and carbonyl groups.[1] In particular, cobalt-catalyzed incorporation of carbon monoxide is interesting as a unique method for the homologation of alkenes, aldehydes, and cyclic ethers, in which $R_3Si–Co(CO)_4$ plays an important role.[2] On the other hand, while hydroformylation is one of the most useful processes for the practical synthesis of aldehydes,[3] no analogous operation toward acetylenic compounds has been developed because of the concomitant formation of undesired products.[4] An excellent precedent is the selective acylation of 1-alkynes at the terminal carbon with the assistance of $Rh_4(CO)_{12}$,[5] or with a stoichiometric amount of $R-Mn(CO)_5$,[6] to give α,β-unsaturated enones. A formal silylformylation of 1-alkynes to give 3-silyl-2-alkenals **2**[7] can represent a useful synthetic approach to these valuable building blocks, due to the ready accessibility and elaboration of alkynes. We have designed a simple formylation reaction of alkynes in the presence of carbon monoxide, employing dimethylphenylsilane (Me_2PhSiH) instead of H_2, and $Rh_4(CO)_{12}$ as catalyst and have found a novel and selective formylation pattern of alkynes to give **2**. We report here the scope and limitations of this new catalytic silylformylation of alkynes.



When an alkyne **1** was allowed to react with 1 equiv each of Me_2PhSiH and Et_3N, using a catalytic amount (1 mol %) of $Rh_4(CO)_{12}$ in benzene solution under CO (30 kg/cm^2) at 100 °C

(1) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981; pp 325–336.

(2) Murai, S.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 837–846.

(3) (a) Pino, P.; Braca, G. *Organic Synthesis via Metal Carbonyls*; Wender, I.; Pino, P., Eds.; Wiley-Interscience: New York, 1977; Vol. 2, pp 41–231. (b) Pruett, R. L. *Advanced Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic Press: New York, 1979; Vol. 17, pp 1–60. (c) Tkatchenko, I.; *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, pp 101–223.

(4) Pino, P.; Braca, G. *Organic Synthesis via Metal Carbonyls*; Wender, I.; Pino, P., Eds.; Wiley-Interscience: New York, 1977; Vol. 2, pp 419–516.

(5) Hong, P.; Mise, T.; Yamazaki, H. *J. Organomet. Chem.* **1987**, *334*, 129–140.

(6) Deshong, P.; Sidder, D. R.; Rybczynski, P. J.; Slough, G. A.; Rheingold, A. L. *J. Am. Chem. Soc.* **1988**, *110*, 2575–2585.

(7) Otera, J.; Mandai, T.; Shiba, M.; Saito, T.; Shimohata, K.; Takemori, K.; Kawasaki, Y. *Organometallics* **1983**, *2*, 332–336.

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