Tetrahedron Letters No. 25, pp 2115 - 2118, 1976. Pergamon Press. Printed in Great Britain.

ALLYLOXYCARBANIONS. CYCLIZATIONS TO VINYL OXETANES.

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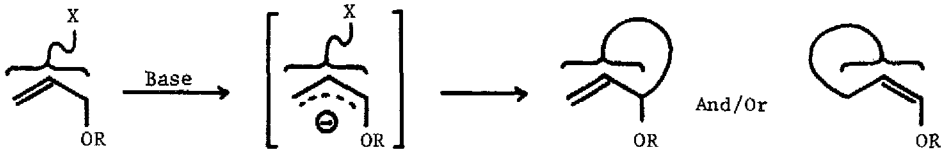
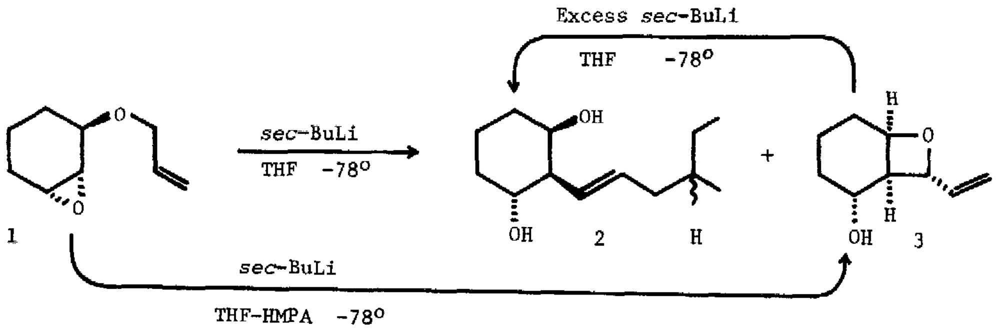
(Received in USA 25 March 1976; received in UK for publication 10 May 1976)

Recently, Evans, Andrews, and Buckwalter[1] and Still and Macdonald[2] independently reported that allylic ethers undergo metalation at low temperatures to form stable, synthetically useful allyloxycarbanions. Since allylic ether deprotonation is extremely fast, utilization of an allylic ether substituted with a suitable electrophilic center should provide a new method for the formation of cyclic carbon-carbon bonds:



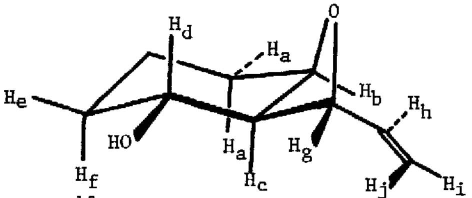
This communication reports the first examples of allyloxycarbanion cyclizations. The reactions studied lead to the unusual vinyl oxetanes[3] 3 and 5 with extremely high regio- and stereoselectivity. The transformation is of special interest since it is one of the few examples of a nonphotochemical oxetane synthesis[4] via carbon-carbon bond formation.[5,6]

When the *trans* epoxy allylic ether[7] 1 was treated with *sec*-butyllithium (THF, -78°), a 1:2 mixture of two substances was produced. These were separated on silica gel (1:4 ethyl acetate:pentane) and were identified as the olefinic diol 2 (ir ν_{max}^{neat}, 3400, 1060, 970 cm^{-1}; nmr δ^{CDCl_3}, 5.58 ($-\overset{H}{C}=\underset{H}{C}-$, 2H, m), 3.98 (H-C-O, 1H, m, $w_{\frac{1}{2}}$ = 10 cps), 3.77 (H-C-O, 1H, td, J = 10, 4 cps), 1.1-2.1 (14H, m), 0.88 (-CH$_3$'s, 6H, m); ms (m/e) parent = 212) and the oxetane 3 (spectral data below).



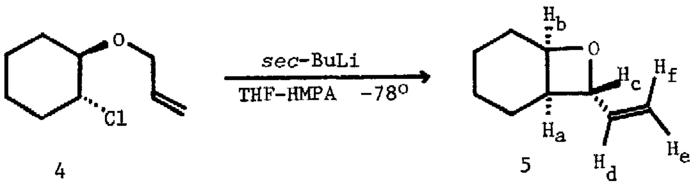
Since the olefinic diol results from S_n2'-like addition of *sec*-butyllithium to 3^8 and requires prior oxetane coordination with Li$^{\oplus}$, strongly coordinating solvents would be expected to increase the yield of the bicyclic product. Thus, cyclization of 1 in THF with 4% HMPA gave a very high yield of the oxetane 3 (96% by VPC and 86% isolated by column chromatography).

Assignment of the hydroxy vinyl oxetane structure for 3 follows from the characteristic spectral properties of the pure material. The infrared spectrum shows peaks (ν_{max}^{neat}) for O-H (3400 cm^{-1}), terminal vinyl (1635, 920, 990 cm^{-1}), and oxetane C-O-C stretch[9] (960 cm^{-1}). The 100-mc nmr suggests the conformation below and displays the following resonances (δ^{CDCl_3}) 6.03 (H_h, 1H, ddd, J_{gh} = 6 cps, J_{hi} = 10 cps, J_{hj} = 17 cps), 5.02-5.34

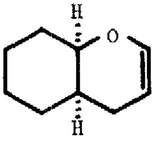


(H_i, H_j, 2H, m), 4.89[10] (H_b, 1H, broad td, J_{ab} = 3 cps, J_{bc} = 7 cps), 4.59[11] (Hg, 1H, broad dd, J_{cg} = 5 cps, J_{gh} = 6 cps), 3.94 (H_d, 1H, td, $J_{cd,de}$ = 5 cps, J_{df} = 7 cps), 2.63 (OH, 1H, broad singlet), 2.41[10] (H_c, 1H, dt, J_{bc} = 7 cps, $J_{cd,cg}$ = 5 cps), 1.1-2.1 (6H, m). The assignments above are in complete accord with decoupling studies and preparation of the acetate (H_d shifts to 4.88 δ) and epoxide (H_g shifts to 4.31 δ) of 3. Although 3 does not give a molecular ion in the mass spectrum, it does show a major peak for the expected loss of acrolein[12] and gives a satisfactory C, H analysis. The bicyclic product is homogeneous on both TLC and VPC, and the sharpness of the nmr signals suggests that 3 is a single stereoisomer. The configuration assigned to the vinyl sidechain is that which would result from the less hindered transition state for cyclization.[13]

Preliminary results indicate that allyloxycarbanion cyclizations are not limited to epoxides. The chloro allylic ether 4[14] cyclized to give a 49% (chromatographed, unoptimized) yield of the vinyl oxetane 5 (ir ν_{max}^{neat}, 1645, 990, 958, 925); nmr δ^{CDCl_3}, 5.90[10]



4 5



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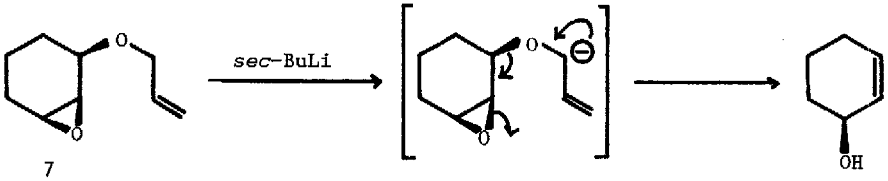
(H_d, 1H, ddd, J = 5.5, 10, 17), 5.06-5.30 (H_c, H_e, H_f, 3H, m), 4.81[10] (H_b, 1H, m), 2.75 (H_a, 1H, ddd, J = 6, 8, 14), 2.3-2.9 (8H, m); MS (m/e) parent-acrolein[12] = 82). NMR examination of the crude reaction mixture revealed no resonance in the vicinity of 6.2-6.4 δ, a region characteristic of the α-proton of enol ethers.[15] Thus, little if any of the γ-cyclized product 6 was formed.

The high preference of these cyclizations for the four-membered ring product is significant and has precedent in epoxy-nitrile cyclizations recently reported by Stork and Cohen.[16] In each case, the preferred pathway is that which leads to the most strained product and requires the least strain for collinear alignment of a nucleophilic orbital and a bond to the leaving group. Both of these observations are consistent with an early transition state.

The collinearity requirement and the strong preference for diaxial epoxide opening virtually rule out the possibility of cyclizing *cis* derivaties such as 7. Thus base treatment of the *cis* epoxy allylic ether 7 gave no detectable enol ether or oxetane, although *trans* 7-oxabicyclo[4.2.0]octanes are known.[17] Instead, 2-cyclohexenol was found to be the major product and could have arisen via the elimination shown below:



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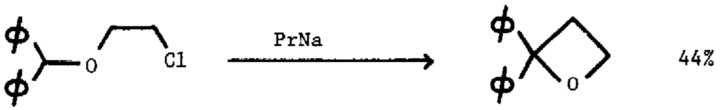
Optimized experimental details for cyclization of 1 are: A solution of 770 mg (5 mmol) of 1, 50 ml of anhydrous THF and 2 ml of anhydrous HMPA was cooled at -78° under nitrogen. The solution was stirred and 6.25 mmol *sec*-butyllithium was added dropwise over a 15-minute period. After five additional minutes, the mixture was quenched with 2 ml of prechilled methanol, poured into 100 ml of pentane, and washed thoroughly with saturated NaCl (4 x 25 ml). The resulting solution was dried (Na_2SO_4) and stripped to a colorless oil (776 mg). Pure 3 was obtained *via* short-column chromatography[18] on 40 gm of silica gel G with 25% ethyl acetate in 40-50° petroleum ether; yield = 660 mg (86%).[19]

REFERENCES AND NOTES

1. D. A. Evans, G. C. Andrews, and B. Buckwalter, *J. Amer. Chem. Soc.*, 96, 5560 (1974).
2. W. Clark Still and T. L. Macdonald, *ibid.*, 96, 5561 (1974).
3. A few other vinyl oxetanes have been reported: Yu. M. Portnyagin and N. E. Pak, *Zh. Org. Khim.*, 7, 1629 (1971) (*Chem. Abstr.*, 75, 140578t (1971)).
4. Oxetane syntheses have been reviewed: (a) S. Searles, Jr., in "Heterocyclic Compounds with Three- and Four-Membered Rings," Part 2, A. Weissberger, Ed., Interscience, New York, N.Y., 1964, p. 983. For more recent work see: (b) J. Biggs, *Tetrahedron Lett.*, 4285 (1975) and references therein.

5. A related cyclization was reported by Searles (Ref. 4a, p. 1043):



The monophenyl derivative gave products from 1,2 elimination.

6. For synthetic uses of oxetanes, see: P. F. Hudrlik and C. -N. Wan, *J. Org. Chem.*, 40, 2963 (1975), and references therein.
7. Compound **1** was prepared from 2-cyclohexenol (1. NaH/THF, allyl bromide (20°, 12 hrs); 2. MCPBA/CH_2Cl_2 (0°, 36 hrs)). The resulting 4:1 mixture of *trans:cis* isomers was separated on silica gel. All compounds reported here were isolated pure as judged by TLC and VPC and gave satisfactory IR, NMR and mass spectra.
8. This reaction was confirmed by the low temperature addition of excess *sec.*-butyllithium to pure **3**. The olefinic diol **2** was isolated in high yield as the only product. Other examples of organolithium addition to oxetane have been reported: S. Searles, *J. Amer. Chem. Soc.*, 73, 124 (1951); M. F. Ansell and B. Gadsby, *J. Chem. Soc.*, 3388 (1958); L. L. Chan and J. Smid, *J. Amer. Chem. Soc.*, 90, 4654 (1968); N. J. Foulger and B. J. Wakefield, *J. Chem. Soc., Perkin Trans. I.* 871 (1974).
9. G. M. Barrow and S. Searles, *J. Amer. Chem. Soc.*, 75, 1175 (1953).
10. The chemical shifts of these protons are characteristic of oxetanes; *cf., inter alia*, C. Schaal, *Bull. Soc. Chim. France*, 3648 (1969); F. Nerdel, H. Kaminsky, and P. Weyerstahl, *Chem. Ber.*, 102, 3679 (1969); Refs. 11 and 12.
11. At first sight, the chemical shift for Hg may seem too far upfield. However, a number of 7-oxabicyclo[4.2.0]octanes show unusually high field resonances for one of the C-8 protons: A. Rosowsky and D. S. Tarbell, *J. Org. Chem.*, 26, 2255 (1961); A. Rosowsky, Ph.D. Thesis, University of Rochester, 1960; E. Wenkert, *et al.*, *J. Amer. Chem. Soc.*, 93, 3208 (1971). The proximate hydroxyl must also be exerting an upfield shift for Hg since the analogous proton in **5** absorbs at $\sim$5.2δ.
12. Other oxetanes show no molecular ion but give intense retro 2 + 2 fragments: J. S. Bradshaw, *J. Org. Chem.*, 31, 237 (1966).
13. This stereochemistry is also in agreement with values reported for oxetane J_{cis} (8.6 cps) and J_{trans} (6.7 cps): N. Lozach and B. Braillon, *Bull. Soc. Chim. France*, 748 (1967); E. Lustig, E. P. Ragelis and N. Duy, *Spectrochim. Acta.*, 23A, 133 (1967).
14. Compound **4** was prepared from cyclohexene (n-chlorosuccinimide, allyl alcohol (40°, 48 hrs.)).
15. L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy to Organic Chemistry," Pergamon, New York, N.Y. 1969, pp 187-189.
16. G. Stork and J. F. Cohen, *J. Amer. Chem. Soc.*, 96, 5270 (1974).
17. Ö. Kovács, *et al.*, *Chem & Ind.*, 1222 (1961); *Chem. Abstr.*, 57, 11135g (1962).
18. B. J. Hunt and W. Rigby, *Chem. and Ind.*, 1868 (1967).
19. This work was supported by Research Corporation.