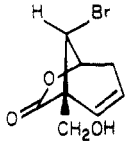
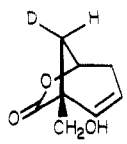
reduction of lactones 2 and 8 was repeated with Bu_3SnD to test whether a deuterium label might be introduced selectively at the pro-C-6 position of shikimate. In fact, both 2 and 8 were cleanly transformed to monodeuterio lactones 5 and 10, respectively. NMR spectroscopy (including decoupling experiments at 300 MHz) proved especially powerful in assigning these structures: H_A which conveniently appeared as a singlet in 2 (δ 4.53) and 8 (δ 4.64) became a doublet in 4 (δ 2.12, J = 11.6 Hz) and 9 (δ 2.38, J = 12.5 Hz). However, after Bu_3SnD reduction, H_A appeared as a slightly broadened singlet in 5 (δ 2.12) and 10 (δ 2.35). Moreover, the extent of deuterium in place of H_A was judged in each case to be no greater than 5% by NMR.[15] This stereochemical outcome could be the result of steric approach control[16] in delivering a hydrogen donor to the radical; alternatively, it may indicate some difference in the thermodynamic stability of the two isomeric radicals. The former seems unlikely since unsubstituted bromo lactone 6 gave results identical with those for 2 and 8 with Bu_3SnD. However, we also observed that the known *anti*-bromo lactone 11[17] was cleanly reduced by Bu_3SnD to 12 with complete inversion of configuration.



11



12

As further proof of its structure, deuterated epoxy alcohol 10 [CIMS, m/e (relative intensity) 158 (M + 1), 100%)] was saponified to 6β-deuterioshikimic acid (1b) whose NMR spectrum matched that of an authentic sample prepared by Hill and Newkome.[18] These studies should now facilitate the synthesis of specifically labeled shikimate and dihydrochorismate[10] analogues for biochemical experiments.

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Supplementary Material Available: Listings of experimental details, physical, and spectral data for key intermediates (4 pages). Ordering information is given on any current masthead page.

(14) L. J. Altman and B. W. Nelson, *J. Am. Chem. Soc.*, 91, 5163 (1969).
(15) Structures 5 and 10 were fully supported by additional NMR, IR, and CIMS data.
(16) In the reduction of certain 6-halopenicillinates, hydrogen is transferred from the less hindered side of the substrate: (a) J. A. Aimetti, E. S. Hamanaka, D. A. Johnson, and M. S. Kellogg, *Tetrahedron Lett.*, 4361 (1979); (b) P. J. Giddings, D. I. John, and E. J. Thomas, *ibid.*, 21, 399 (1980).
(17) B. Ganem, G. W. Holbert, L. B. Weiss, and K. Ishizumi, *J. Am. Chem. Soc.*, 100, 6483 (1978).
(18) R. K. Hill and G. R. Newkome, *J. Am. Chem. Soc.*, 91, 5893 (1969); ^1H NMR (D_2O, 300 MHz) δ 6.63 (dd, 1 H, J = 4, 1.5 Hz), 4.60 (s, HOD), 4.26 (m, 1 H), 3.84 (dd, 1 H, J = 8, 5 Hz), 3.59 (dd, 1 H, J = 8, 4 Hz), 2.53 (br s, 1 H).

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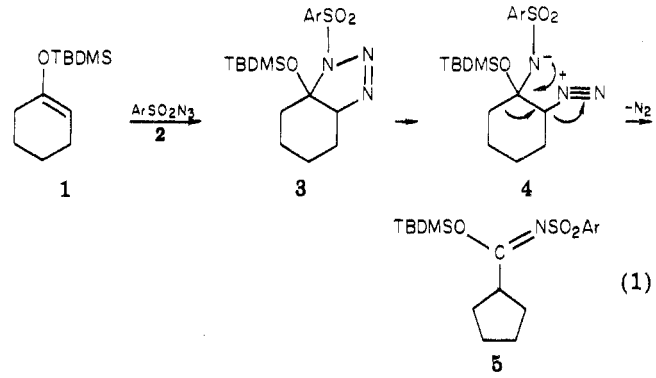
Organic Reactions at High Pressure. Dipolar Cycloaddition-Ring Contraction Reactions of Hindered Silyl Enol Ethers and Arylsulfonyl Azides[1,2]

Summary: Dipolar cycloaddition of arylsulfonyl azides with sterically congested silyl enol ethers at 15 kbar (1.5 GPa) in acetonitrile/methylene chloride cleanly affords good yields of one-carbon ring-contracted products.

Sir: In 1973, a ring contraction[3] was reported involving dipolar cycloaddition of arylsulfonyl azides with unsubstituted cyclic enol ethers to afford good yields of sulfonamide products. Subsequent work in our laboratories directed toward construction of the ophiobolin nucleus[4] demonstrated that the method is sensitive to the steric environment surrounding the electron-rich double bond. Since dipolar cycloadditions are known to exhibit a negative $\Delta V^{\ddagger}$,[5] a rate enhancement is anticipated under elevated pressure conditions. The present study describes the successful application of high-pressure chemistry to the ring contraction of a variety of silyl enol ethers possessing varying degrees of substitution.

The reaction, formulated in eq 1, reportedly involves



1 3 4 5 (1)

regioselective 1,3-dipolar azide addition to the electron-rich double bond to give a Δ^2-1,2,3-triazoline 3[6] which fragments stepwise via a diazonium betaine 4 to give the water-sensitive imidate ester 5. The regioselectivity of the addition to the polarized enol π bond assures that ring contraction occurs predictably with σ bond migration from the α to the β enol carbon. This constitutes an advantage of this procedure over Favorskii-type rearrangements.[7]

The reaction was performed on the *tert*-butyldimethylsilyl (TBDMS) enol ethers[8] which exhibited greater stability than the corresponding trimethylsilyl (Me_3Si) enol ethers in cases where prolonged heating was required. In contrast to enamines,[9] known to undergo this ring contraction without pressure, silyl enol ethers allow for greater control of regiospecificity in enol formation and afford cleaner products. It was observed that the thermodynamic

(1) This work was supported in part by National Science Foundation Grant No. CHE-810-2938.
(2) NIH Postdoctoral Fellow, 1981 to present.
(3) (a) Wohl, R. A. *Tetrahedron Lett.* 1973, 3111. (b) Wohl, R. A. *Helv. Chim. Acta* 1973, *56*, 1826.
(4) Dauben, W. G.; Hart, D. J. *J. Org. Chem.* 1977, *42*, 922.
(5) Representative $\Delta V^{\ddagger}$ determinations of 1,3-dipolar cycloadditions are given in: Isaacs, N. S. "Liquid Phase High Pressure Chemistry"; Wiley-Interscience: New York, 1981; pp 222, 227.
(6) (a) The first report of Δ^2-1,2,3-triazoline formation was in: Wolff, L. *Justus Liebigs Ann. Chem.* 1912, *394*, 23. (b) For a review of this reaction see: L'Abbé, G. *Chem. Rev.* 1969, *69*, 345. (c) See also: Sheradsky, T. In "The Chemistry of the Azido Group"; Patai, S., Ed.; Wiley-Interscience: New York; pp 359, 373. (d) Lwowski, W. *Ibid.*, pp 529–31.
(7) For a review of the Favorskii rearrangement, see: Kende, A. S. *Org. React.* 1960, *11*, 261.

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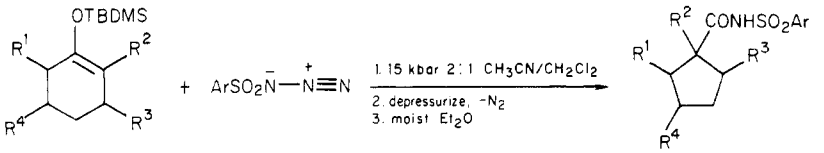
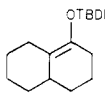
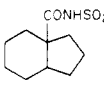
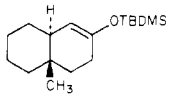
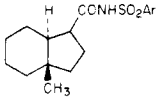
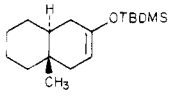
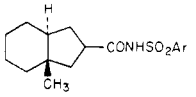
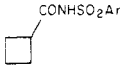
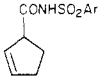
Table I. Ring Contraction of Substituted Cyclohexanone Enol Ethers[a,b]



					15 kbar			1 bar (sealed tube)		
run	R_1	R_2	R_3	R_4	time, h	temp, °C	% yield	time, h	temp, °C	% yield
1	H	H	H	H	36	18	86.5	96	75	65.6
2	CH_3	H	H	H	36	18	84.2	96	75	49.8
3	H	H	CH_3	CH_3	48	18	77.9			
4	H	CH_3	H	H	18	55	80.8			
5	CH_3	CH_3	H	H	20	55	62.1	96	75	13.2
6	β-*i*-Pr	H	α-CH_3	H	72	65	78.6	96	75	0.0

[a] TBDMS = *tert*-butyldimethylsilyl, and Ar = *p*-bromophenyl. [b] All compounds gave satisfactory spectral and analytical data. Yields are isolated.

Table II. Ring Contraction of Decalone Enol Ethers and Other Examples at 15 kbar[a,b]

run	starting material	product	time, h	temp, °C	yield, % (isol)
1			36	55	73.6
2[c]			96 48	18 55	74.6 67.4
3			48 48	18 55	33.1 72.5
4[d]			24	18	60.2
5			36	18	12.0
		$ArSO_2NH_2$			61.8
		PhOTBDMS			53.1

[a] TBDMS = *tert*-butyldimethylsilyl, and Ar = *p*-bromophenyl. [b] All compounds gave satisfactory spectral and analytical data. [c] A comparison run at 50 °C, 72 h, and 1 bar gave 35.0% yield. [d] Product could not be obtained in >90% purity.

enol acetates[8c] of unsymmetrical ketones used as precursors to the more substituted TBDMS enol ethers[8d] were inert to the reaction conditions, thus confirming the importance of the electron-rich nature of the double bond to the success of the reaction. Among the arylsulfonyl azides studied [Ar = *p*-Br, *p*-CH_3-, *m*-NO_2-, and 2,4-$(NO_2)_2$Ph], the *p*-bromobenzenesulfonyl azide proved superior due to the ease in isolating the highly crystalline products. The Me_3Si azide did not undergo cycloaddition, demonstrating the requirement for electron-withdrawing substituents on the 1,3-dipole.

The problem of accommodating the 22.4 mL of nitrogen gas theoretically released per millimole was resolved by running the reactions in sealed evacuated Teflon tubes filled to 20% of the total volume with 2:1 acetonitrile/methylene chloride solutions of equimolar amounts of enol ether and azide (1.0 mL for 1.0 mmol of reactants). From the safety standpoint, all individual reactions were kept to the 1-mmol scale; the present apparatus, described previously,[10] permits the simultaneous pressurization of three 1.0-mmol reactions. The tubes were pressurized at 15 kbar (1.5 GPa) for 18–96 h at 18–65 °C, and then depressurized (nitrogen was released during decompression), and the reaction mixture was concentrated. Since the imidate ester could not be isolated without contamination by the sulfonamide, the mixture was treated with moist ether from which the analytically pure sulfonamide crystallized as a mixture of stereoisomers.

The results of the present study are summarized in Tables I and II. The series of cyclohexanone enol ethers in Table I illustrates the power of high-pressure conditions

(8) (a) The lithium enolates (prepared from 1.1 equiv of LDA) were quenched with a 4:1 THF/HMPA solution of 1.5 equiv of *tert*-butyldimethylsilyl chloride and 1.5 equiv of triethylamine at −78 °C and stirred with warming to room temperature during 8 h. (b) The enolate derived from Li/liquid NH_3 reduction of 10-methyl-1(9)-octalin-2-one was prepared by using the general procedure of Stork and Singh (Stork, G.; Singh, J. *J. Am. Chem. Soc.* **1974**, *96*, 6181) and quenched as in ref 8a. (c) House, H. O.; Gall, H.; Olmstead, H. M. *J. Org. Chem.* **1971**, *36*, 236; (d) Tetrasubstituted TMBDS enol ethers were generated from the enol acetates by the procedure of House and Umen (House, H. O.; Umen, M. J. *J. Org. Chem.* **1973**, *38*, 1000) and quenched as in ref 8a.

(9) (a) Fusco, R.; Bianchetti, G.; Pocar, D. *Gazz. Chim. Ital.* **1961**, *91*, 933. (b) Schribner, R. M. *Tetrahedron Lett.* **1967**, 4737.

(10) Dauben, W. G.; Krabbenhoft, H. O. *J. Org. Chem.* **1977**, *42*, 282.

in overcoming steric inhibition. The enol ether derived from *l*-menthone (entry 6, Table I) provided the most demanding test and offered the most dramatic comparison, showing no ring-contracted products at 1 bar and 79% ring-contracted products at 15 kbar under similar thermal conditions. Contraction of the readily available *trans*-decalone enols shown in Table II demonstrates the utility of this technique as a strategy for obtaining the *trans*-hydrindane system with predictable positioning of the residual functionality. The reaction is also seen to be applicable to the five- to four-membered-ring contraction, but this product could not be obtained in >90% purity. Finally, the cyclohexadiene enol ether gives predominantly aromatization with only 12% of ring-contracted product. Although the six- to five-membered-ring conversion appears the most useful, the method has been reported on larger unsubstituted rings,[3] and pressure would likely find utility in contracting more highly substituted large-ring enols.

These investigations show that the pressure variable can be a valuable tool in the arsenal of the synthetic organic chemist, offering an exceptionally mild method for accelerating sluggish bond-forming reactions on sensitive and sterically crowded substrates. In the present study, we have overcome steric factors to prepare a number of substituted cyclopentanes and hydrindanes otherwise inaccessible by employing standard pressure conditions.

Acknowledgment. We are indebted to Dr. Walter Eschenmoser for his preliminary study of this pressurized reaction sequence.

Registry No. 1, 62791-22-4; 1 (6-CH_3), 20152-34-5; 1 (3,5-(CH_3)$_2$), 83681-03-2; 1 (4-CH_3), 20152-33-4; 1 (2,6-(CH_3)$_2$), 62791-24-6; 1 (3-α-CH_3-6-β-*i*-Pr), 83681-04-3; **2** (Ar = *p*-bromophenyl), 6647-76-3; *N*-[(*p*-bromophenyl)sulfonyl]cyclopentanecarboxamide, 51584-37-3; *N*-[(*p*-bromophenyl)sulfonyl]-2-methylcyclopentanecarboxamide, 83681-05-4; *N*-[(*p*-bromophenyl)-sulfonyl]-2,4-dimethylcyclopentanecarboxamide, 83681-06-5; *N*-[(*p*-bromophenyl)sulfonyl]-1-methylcyclopentanecarboxamide, 83681-07-6; *N*-[(*p*-bromophenyl)sulfonyl]-1,2-dimethylcyclopentanecarboxamide, 83681-08-7; *N*-[(*p*-bromophenyl)-sulfonyl]-2-isopropyl-5-methylcyclopentanecarboxamide, 83681-09-8; 1-[(*tert*-butyldimethylsilyl)oxy]-2,3,4,4a,5,6,7,8-octahydronaphthalene, 83681-10-1; *trans*-2-[(*tert*-butyldimethylsilyl)-oxy]-4a-methyl-3,4,4a,5,6,7,8,8a-octahydronaphthalene, 83681-11-2; *trans*-2-[(*tert*-butyldimethylsilyl)oxy]-4a-methyl-1,4,4a,5,6,7,8,8a-octahydronaphthalene, 83681-12-3; 1-[(*tert*-butyldimethylsilyl)oxy]-1-cyclopentene, 68081-15-2; 1-[(*tert*-butyldimethylsilyl)oxy]-1,5-cyclohexadiene, 71106-34-8; *N*-[(*p*-bromophenyl)sulfonyl]hydrindan-3a-carboxamide, 83681-13-4; *N*-[(*p*-bromophenyl)sulfonyl]-3a-methylhydrindan-1-carboxamide, 83681-14-5; *N*-[(*p*-bromophenyl)sulfonyl]-3a-methylhydrindan-2-carboxamide, 83681-15-6; *N*-[(*p*-bromophenyl)sulfonyl]butanecarboxamide, 83681-16-7; *N*-[(*p*-bromophenyl)sulfonyl]cyclopent-2-enecarboxamide, 83681-17-8.

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