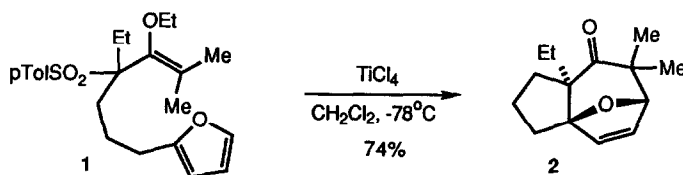


ALLYL CATION STEREOCHEMISTRY IN THE INTRAMOLECULAR 4+3 CYCLOADDITION REACTION

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Summary: Initial allyl cation geometry appears to be irrelevant with respect to the stereochemistry of cycloadducts in the intramolecular 4+3 cycloaddition of alkoxyallylic cations derived from alkoxyallylic sulfones.

We recently reported new methodology for the execution of intramolecular 4+3 cycloadditions in which alkoxyallylic sulfones served as precursors to the requisite alkoxyallylic cations (Equation 1).¹⁻⁴ In our continuing

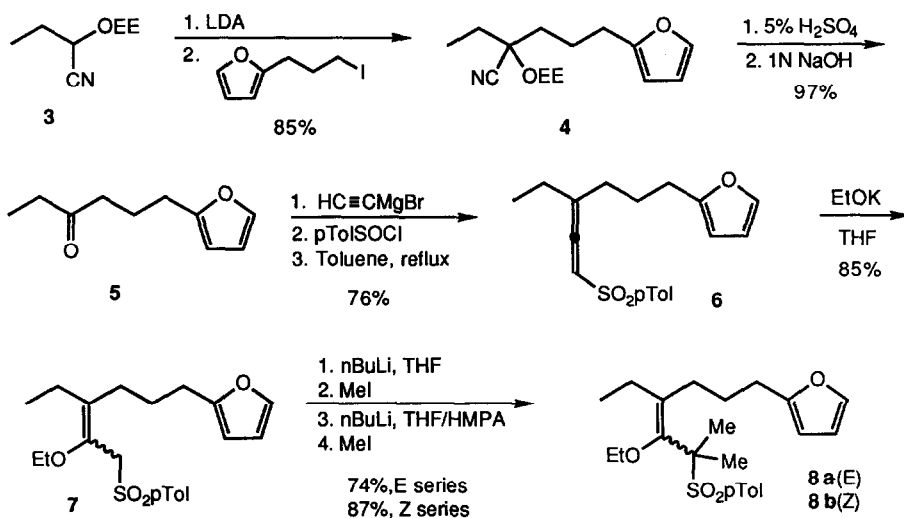


Equation 1

studies of this reaction we became interested in the effect of allyl cation stereochemistry on the course, particularly the stereochemical course, of this reaction.

Our initial studies allowed no clear understanding of the effects of allyl cation geometry on this reaction since both cation configurations were available from the alkoxyallylic sulfone. A system in which at least the initial configurations could be determined had to be prepared. The synthesis is shown in Scheme 1. Treatment of the protected cyanohydrin of propionaldehyde⁵ with LDA followed by alkylation with 2-(3-iodopropyl)furan⁶ gave 4 in 85% yield. Hydrolysis afforded ketone 5 in virtually quantitative yield.⁸ Condensation of 5 with ethynyl-magnesium bromide followed by sulfinate ester formation with p-toluenesulfinyl chloride⁹ and thermolysis gave the allenic sulfone 6 in 76% overall yield.^{10,11} Nucleophilic addition of ethoxide gave an 85% yield of alkoxyallylic sulfone 7 as a 1:1 mixture of E and Z isomers.¹² These isomers could be separated using preparative HPLC.¹³ The stereochemical assignments of these isomers were secured by NOESY. Either isomer of 7 could be alkylated twice with methyl iodide to give 8a or 8b, the cycloaddition precursors.¹⁴

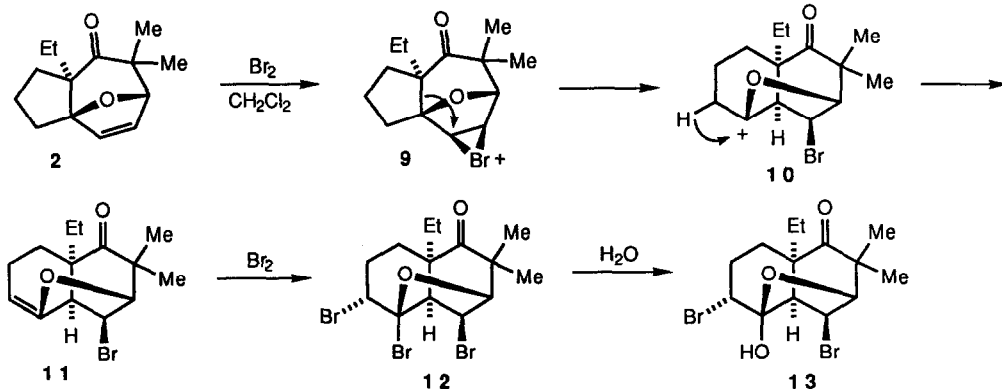
Treatment of either isomer of 8 with TiCl₄ in CH₂Cl₂ at -78°C gave 2 in 58% yield after chromatographic purification. It is interesting and important that both isomers lead solely to the same product and in the same yield. This observation is corroborated by inspection of molecular models which suggests that the lowest energy transition structures for 4+3 cycloaddition lead to 2 regardless of allyl cation geometry. Somewhat disturbing is the finding that the transformation of 8 to 2 takes place in 20% lower yield than the conversion of 1 to 2. This suggests that a



Scheme 1

common intermediate may not be produced for both cycloaddition precursors.

The structure of **2** was initially based on precedent from our own work and the literature.^{1,4} Attempts to deduce stereochemical information using *n*Oe were unsuccessful and ultimately we turned to X-ray analysis of a derivative of **2** to establish relative stereochemistry. Treatment of **2** with bromine in CH_2Cl_2 at -78°C followed by warming to room temperature produced the decalin derivative **13** as shown in Scheme 2. Apparently, bromonium



Scheme 2

ion formation is followed by a 1, 2 shift to produce oxonium ion **10**. Loss of a proton, followed by a second bromination and hydrolysis upon work-up gives **13** in 83% yield after recrystallization. X-ray analysis confirmed the structure of **13** and established the expected relative stereochemical relationships in **2** (Figure 1).¹⁵ Such rearrangements should offer unique opportunities in the synthesis of carbocycles from cycloadducts such as **2**.¹⁶

In summary, we have shown that the initial geometry of the allylic cation in intramolecular 4+3 cycloadditions is irrelevant with respect to the yield and stereochemistry of the cycloadduct obtained. Whether this points to rapid

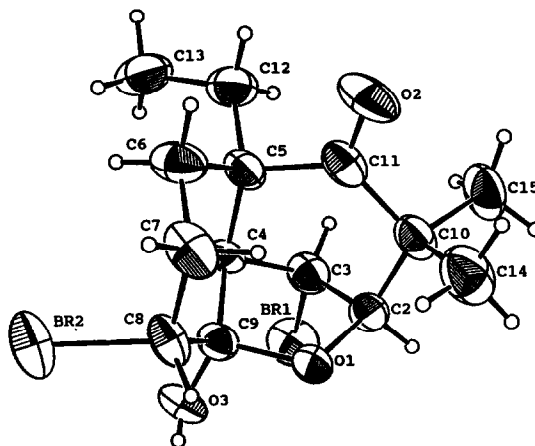


Figure 1

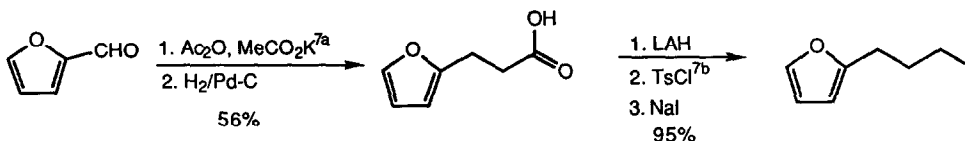
rotation of an allylic cation intermediate or whether a discrete allyl cation exists at all is currently being addressed through studies on relative asymmetric induction.¹⁷

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References and Notes

- (1) Harmata, M.; Gamlath, C.B. *J. Org. Chem.* **1988**, *53*, 6154.
- (2) For a review of sulfones as "chemical chameleons" by the developer of this concept, see: Trost, B.M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 107.
- (3) For reviews of the 4+3 cycloaddition reaction, see: (a) Hoffmann, H.M.R. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 1. (b) Mann, J. *Tetrahedron* **1986**, *42*, 4611. (c) Noyori, R.; Hayakawa, Y. *Org. React.* **1983**, *29*, 163.
- (4) For examples of intramolecular 4+3 cycloaddition reactions, see: (a) Noyori, R.; Nishizawa, M.; Shimizu, F.; Hayakawa, Y.; Maruoka, K.; Hashimoto, S.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1979**, *101*, 220. (b) Hoffmann, H.M.R.; Henning, R. *Helv. Chim. Acta* **1983**, *66*, 828. (c) Föhlisch, B.; Herter, R. *Chem. Ber.* **1984**, *117*, 2580. (d) Schultz, A.G.; Macielag, M.; Plummer, M. *J. Org. Chem.* **1988**, *53*, 391. (e) Giguere, R.J.; Duncan, S.M.; Bean, J.M.; Purvis, L. *Tetrahedron Lett.* **1988**, 6071.
- (5) Young, S.D.; Buse, C.T.; Heathcock, C.H. *Org. Syn.* **1985**, *63*, 79.

(6) 2-(3-Iodopropyl)furan was prepared by the following sequence:



(7) (a) Vogel, A.I. "Vogel's Textbook of Practical Organic Chemistry"; 5th ed. Longman: Essex, 1989; p 1039.

(b) Kabalka, G.W.; Varma, M., Varma, R.S., Srivastava, P.C.; Knapp Jr., F.F. *J. Org. Chem.* **1986**, *51*, 2386.

(8) Attempts to add ethylmagnesium bromide to 3-furylpropionitrile gave at best only low yields of 5.

(9) Kurzer, F. "Organic Syntheses Collective Vol. 4"; Wiley: New York, 1963; p 937.

(10) (a) Braverman, S.; Mechoulam, H. *Tetrahedron* **1974**, *30*, 3883. (b) Smith, G.; Stirling, C.J.M. *J. Chem. Soc. C* **1971**, 1530.

(11) The most capricious step in this sequence was the thermolysis of the sulfinate to produce the allenic sulfone. The variable yield of the thermolysis can be attributed to the formation of a number of as yet unidentified side products perhaps derived from reaction of the allene with the furan.

(12) (a) Stirling, C.J.M. *J. Chem. Soc.* **1964**, 5856. (b) Denmark, S.E.; Harmata, M.A.; White, K.S. *J. Org. Chem.* **1987**, *52*, 4031. (c) Barre, V.; Massias, F.; Uguen, D. *Tetrahedron Lett.* **1989**, 7389.

(13) Column: Rainin Dynamax, 12 μm silica, 21.4x250 mm. Mobile phase: CH₂Cl₂, 9 ml/min.

(14) The final alkylation step requires the presence of HMPA to avoid elimination of the ethoxy group.

(15) MW=380.13; Space Group: P2₁/C (# 14); a = 10.900(6)Å, b = 9.054(4)Å, c = 16.565(5)Å, β = 106.41(4)°; V = 1568(1)Å³; Z = 4; D_{calc} = 1.610; Radiation = MoKα (λ = 0.71073)Å; μ = 51.1cm⁻¹; F(000) = 760; Temperature = 23+/-1o; Final R = 0.048 for 1428 reflections with I>3σ(I).

(16) For some examples of related rearrangements, see: (a) Keay, B.A.; Rogers, C.; Bontront, J.-L.J. *J. Chem. Soc. Chem. Commun.* **1989**, 1782. (b) Archer, D.A.; Bromidge, S.M.; Sammes, P.G. *J. Chem. Soc. Perkin Trans. 1* **1988**, 3223. (c) Sammes, P.G.; Street, L.J.; Whitby, R.J. *Ibid.* **1986**, 281.

(17) All new compounds exhibited acceptable ¹H and ¹³C NMR and IR spectra as well as satisfactory combustion or exact mass data. All yields are for chromatographically purified materials.

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