Tetrahedron Letters No. 30, pp 2595 - 2598, 1974. Pergamon Press. Printed in Great Britain.

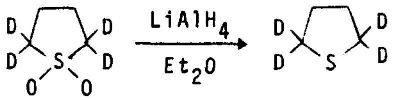
OBSERVATIONS ON THE MECHANISM OF REDUCTION OF SULFONES TO SULFIDES

William P. Weber*, Phillip Stromquist, and Thomas Isami Ito
Department of Chemistry
University of Southern California
Los Angeles, California 90007

(Received in USA 2 May 1974; received in UK for publication 17 June 1974)

The ease of reduction of sulfones to sulfides by treatment with $LiAlH_4$ has been observed to be highly dependent on the structure of the sulfone.[1] Thus, four and five-membered cyclic sulfones are rapidly reduced to the corresponding sulfides with $LiAlH_4$ in ether at 35°C. On the other hand, six-membered cyclic sulfones and open chain sulfones require much more vigorous conditions. In a classic experiment Whitney and Cram showed that reduction of optically active 2-methyl-2,3-dihydrobenzothiophene-2-d_1-1,1-dioxide with $LiAlH_4$ leads to the corresponding sulfide with neither loss of deuterium nor optical activity.[2] Thus reduction of five-membered cyclic sulfones does not involve formation of a carbanion alpha to the sulfone group, and therefore probably occurs by nucleophilic attack of coordinated hydride on sulfur leading to displacement of oxygen as the critical step.

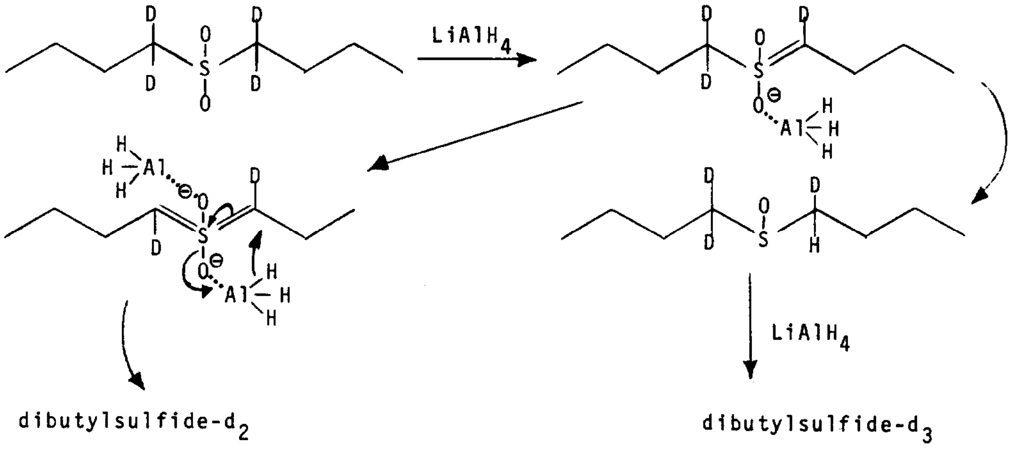
As expected, we find that reduction of thiacyclopentane-2,2,5,5-d_4-1,1-dioxide[3] with $LiAlH_4$ in ether yields the corresponding thiacyclopentane-2,2,5,5-d_4 in virtually quantitative yield.[4]



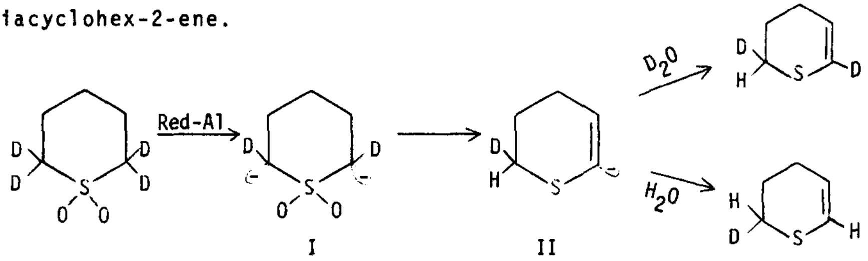
However, the reason for the extreme difficulty in reduction of six-membered cyclic sulfones and open chain sulfones remains unclear. We should like to report experiments that indicate that the species undergoing reduction is <u>not</u>

the sulfone but rather the α-monoanion or the α,α'-dianion of the sulfone.

Treatment of dibutylsulfone [5] at 25°C with Red-Al, i.e. sodium bis-(2-methoxyethoxy)aluminum hydride, in benzene results in a rapid evolution of two equivalents of hydrogen. However, reduction has not occured at this stage but merely dianion formation since addition of this solution to D_2O/D^+ yields not dibutylsulfide [6] but rather dibutylsulfone-d_2. Deuterium content was determined by nmr and by mass spectrometry.[7] Both methods indicate greater than 90%-d_2. Similar results have been observed with $LiAlH_4$ except that evolution of the second equivalent of hydrogen is much slower and incomplete. Dianions of dialkyl sulfones have been previously generated by treatment of the sulfone with n-butyl lithium.[8] Reduction of dibutylsulfone-d_4 with $LiAlH_4$ in refluxing purified dioxane yields dibutylsulfide (8%-d_1,50%-d_2, and 42%-d_3 by mass spectrometry[7]). Possibly $LiAlH_4$ reduction of the monoanion occurs competitively with dianion formation. A mechanism consistent with these results is proposed in scheme 1.



Reaction of thiacyclohexane-1,1-dioxide [9] with Red-Al in benzene at room temperature leads to rapid (1 hour) evolution of two equivalents of hydrogen. However, reduction has not occurred at this stage but merely dianion formation. since addition of the solution to D_2O/D^+ yields not thiacyclohexane, but rather thiacyclohexane-2,6-d_2-1,1-dioxide. Reduction of thiacyclohexane-1,1-dioxide with $LiAlH_4$ in refluxing dioxane or refluxing Red-Al in benzene for 12 hours yields two volatile products in a ratio of 4:1. The expected product,[1] thiacyclohexane[9] is isolated in 6% yield. The major volatile product is found to be thiacyclohex-2-ene[10-12] isolated in 25% yield. Evidently, thiacyclohexane-1,1-dioxide is more easily reduced than dibutylsulfone since while both are reduced by $LiAlH_4$ in refluxing dioxane, only thiacyclohexane-1,1-dioxide is reduced by Red-Al in refluxing benzene. Reduction of thiacyclohexane-2,2,6,6-d_4-1,1-dioxide with Red-Al in refluxing benzene yields thiacyclohex-2-ene-6-d_1 by nmr (9%-d_0, 91%-d_1 by mass spectrometry[7]) if the reaction is quenched with H_2O, but thiacyclohex-2-ene-2,6-d_2 by nmr (4%-d_0,35%-d_1, and 61%-d_2 by mass spectrometry[7]) and thiacyclohexane-2,6-d_2 by nmr if the reaction is quenched with D_2O. Similar results have been obtained using $LiAlH_4$ in dioxane as reducing agent followed by reaction with either H_2O or D_2O. Clearly, the sulfone dianion (I) is the first formed reaction intermediate while the final intermediate is an alpha vinyl sulfide anion (II) which on reaction with H_2O yields thiacyclohex-2-ene.



Studies to elucidate more completely the reaction pathways leading to reduction of sulfones are in progress. Certainly one major difference between a cyclic six-membered sulfone and an open chain sulfone is the existence of axial hydrogens in the cyclic compound.

References:

1. F. G. Bordwell and W. H. McKellin, *J. Am. Chem. Soc.*, **73**, 2251 (1951).
2. T. A. Whitney and D. J. Cram, *J. Org. Chem.*, **35**, 3964 (1970).
3. S. Kunichika, S. Oka, M. Yokoi, and T. Nakashima, *J. Chem. Soc. Japan. Ind. Chem. Sect.*, **56**, 931 (1953).
4. L. Brandsma and H. Wijers, *Rec. Trav. Chim.*, **82**, 68 (1963).
5. D. Barnard, *J. Chem. Soc.*, **1957**, 4547.
6. H. LeB Gray and G. O. Gutekunst, *J. Am. Chem. Soc.*, **42**, 856 (1920).
7. K. Bieman, " Mass Spectrometry - Organic Chemical Applications", McGraw-Hill, New York, N.Y., 1962; see Chapter 5 for treatment of data for deuterium labeled compounds.
8. L. A. Paquette, R. H. Meisinger, and R. Gleiter, *J. Am. Chem. Soc.*, **95**, 5414 (1973).
9. L. Bateman, J. I. Cunnen, and J. Ford, *J. Chem. Soc.*, **1957**, 1539.
10. R. F. Naylor, *J. Chem. Soc.*, **1949**, 2749.
11. W. E. Parham, L. Christensen, S.H. Groen, and R. M. Dodson, *J. Org. Chem.*, **29**, 2211 (1964).
12. Thiacyclohex-2-ene was purified by glpc on a 1/4" X 20' Carbowax 20 M at 170°C. It had the following spectral properties: ir 1603 cm^{-1}, nmr, m(4H) 2.0δ, t(2H) 2.73δ , J = 8Hz, d of t (1H) 5.55δ ,J = 10 Hz, J = 4 Hz, d(1H) 5.87δ. Irradiation of the multiplet at 2.0δ causes the d of t at 5.55δ to collapse to a double J = 10 Hz. Mass spectra: parent ion at m/e = 100.

Acknowledgements: This is supported part by a grant from the Air Force Office of Scientific Research - grant number 73-2424 and a grant from the National Science Foundation - grant number GP-40331X.