Tetrahedron Letters, Vol.31, No.16, pp 2233-2234, 1990
Printed in Great Britain

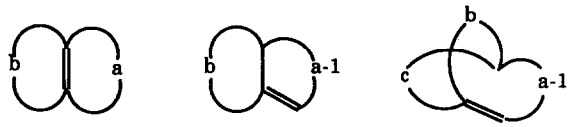
0040-4039/90 $3.00 + .00
Pergamon Press plc

THE PREPARATION AND REARRANGEMENT OF BRIDGEHEAD ENONES FROM SULFOXIDES UNDER MILD REACTION CONDITIONS

George A. Kraus* and Jeff Hansen
Department of Chemistry, Iowa State University, Ames, IA 50011

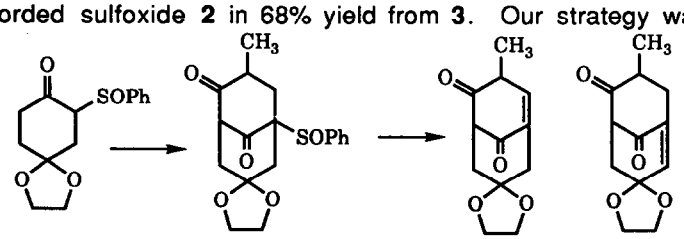
Summary: The conversion of sulfoxide **2** into enone **5** proceeds via a regiospecific sulfoxide elimination followed by a bridgehead enone rearrangement.

The synthesis of polycyclic ring systems can be facilitated by strategies incorporating bridgehead intermediates. Williams utilized bridgehead carbanion chemistry in his clever synthesis of bicyclomycin.[1] Magnus made use of a bridgehead enone in his classic synthesis of the kopsane alkaloids.[2] We employed both bridgehead enones and bridgehead carbocations in our synthesis of lycopodine.[3] Recently, Warner has published a thorough review of bridgehead enone chemistry which nicely collates both synthetic and mechanistic advances.[4] The development of new bridgehead strategies is dependent on the continued investigation of bridgehead intermediates. While bridgehead enones of type A and type B have been well studied, much less is known about the reactions of type C enones[5] with nucleophiles, particularly when the carbonyl is in a one-carbon bridge.



Type A Type B Type C

As part of a concerted effort to understand bridgehead reactivity, we examined synthetic routes to **1**. Keto sulfoxide **2** appeared to be a logical precursor to **1**. It was prepared by the reaction of keto sulfoxide **3** with methacrolein and DBU. The best yields were obtained when methacrolein in acetonitrile was added dropwise to a 0.1 M solution of acetonitrile containing **3** and DBU. Oxidation of the keto alcohol to the diketone with Jones' reagent afforded sulfoxide **2** in 68% yield from **3**. Our strategy was to generate the



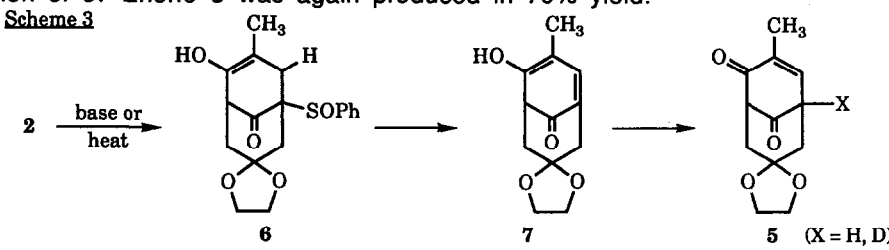
3 2 1 4

bridgehead enone in situ in the presence of primary amines. The primary amines would function as both trapping agents and as interceptors of phenylsulfenic acid.

In principle, two isomeric enones **1** and **4** could be formed, depending on the direction of sulfoxide elimination. Heating sulfoxide **2** in the presence of four equivalents of tert-butyl amine at 140°C for 20 h afforded enone **5** in 62% yield. The structure was supported by a proton NMR resonance at 1.89 (bs) for the methyl group and at 6.87 (dq) for the olefinic hydrogen atom. Enone **5** probably was formed by isomerization of **1**. The same result, formation of enone **5**, was obtained with other amines.

Surprisingly, there was no evidence for the products resulting from the generation of enone **4**. The regiochemistry of sulfoxide eliminations in monocyclic systems is often dictated by electronic factors. For example, allylic hydrogens or hydrogens on carbon atoms adjacent to a carbonyl group promote regioselective sulfoxide eliminations.[6] There was no clear driving force for unidirectional elimination with sulfoxide **2**. We next heated sulfoxide **2** in toluene for 20 h at 150°C to determine whether an amine was required for the formation of **5**. Enone **5** was again produced in 70% yield.

Scheme 3



The unusually facile generation of enone **5** by a regioselective sulfoxide elimination might be rationalized as proceeding via intermediates **6** and **7**. Hydroxydiene **7** is a novel bridgehead unit which has not been observed or even invoked in mechanistic studies of bridgehead intermediates. In order to obtain support for the above mechanism, the sulfoxide elimination was conducted in the presence of $tBuND_2$ or D_2O. The monodeuterio product **5** (X=D) was cleanly obtained, as evidenced by the NMR and the high resolution mass spectrum. Attempts to trap **7** with I_2 and PhSeSePh failed.

This elimination/rearrangement sequence provides a direct route to **5**, which is an intermediate for our synthesis of selagine. The enolization-promoted regiospecific sulfoxide elimination concept may be useful in many other systems.

REFERENCES

1. R. M. Williams, R. W. Armstrong, J. S. Dung *J. Am. Chem. Soc.*, **1984**, *106*, 5748.
2. R. Magnus, T. Gallagher, P. Brown, J. C. Huffman *J. Am. Chem. Soc.*, **1984**, *106*, 2105.
3. G. A. Kraus, Y.-S. Hon *J. Am. Chem. Soc.*, **1985**, *107*, 4341.
4. P. Warner *Chem. Rev.*, **1989**, 1067.
5. G. Szeimies, Reactive Intermediates, R. A. Abramovitch, ed. (Plenum Press, NY, 1983), p. 299.
6. C. Kingsbury, D. Cram *J. Am. Chem. Soc.*, **1960**, *82*, 1810.

(Received in USA 13 December 1989)