Tetrahedron Letters No. 40, pp 3815 - 3818. 0040-4039/79/1001-3815$02.00/0

ELIMINATION REACTIONS IN DIMETHYL SULFOXIDE SOLUTION. THE EFFECTIVE BASE WITH POTASSIUM *tert*-BUTOXIDE.

Robert D. Bach* and James W. Knight
Department of Chemistry
Wayne State University
Detroit, Michigan 48202

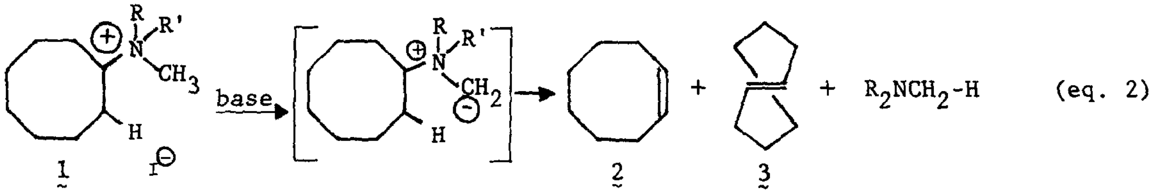
Deuterium labeling studies have established that elimination of a cyclooctylammonium iodide with dimsyl anion in DMSO proceeds through an ylide intermediate while elimination with $KOC(CH_3)_3$ in DMSO involves an E2 mechanism. The effective base with $KOC(CH_3)_3$/DMSO is shown to be the alkoxide ion.

The use of dipolar aprotic solvents in elimination reactions has assumed increased importance with the recognition of cation-anion base pair effects.[1] Both dimsyl anion, the conjugate base of dimethyl sulfoxide (DMSO), and solutions of potassium *tert*-butoxide in DMSO are frequently used in base-catalyzed reactions. However, conflicting reports about the actual concentration of dimsyl anion in the latter base-solvent system have appeared and as a result the effective base in this medium remains a subject of speculation. Ritchey[2] has suggested that the concentration of dimsyl anion should be very low (eq. 1), while Brauman[3]

$$\underline{\text{tert}}\text{-Bu}\bar{\text{O}}\text{K}^+ + CH_3SOCH_3 \rightleftarrows \underline{\text{tert}}\text{-BuOH} + CH_3SOCH_2^-K^+ \qquad \text{(eq. 1)}$$

reported an equilibrium constant two orders of magnitude higher and suggested that the actual concentration of dimsyl anion is 0.2 M at equilibrium when the initial [*tert*-BuOK]=0.57 M. This discrepancy has been attributed to aggregation effects that are concentration dependent.[3,4]

In our previous elimination studies[5] we showed that strong bases such as NH_2^-/NH_3, and and RLi react with cyclooctylammonium halides by an intramolecular α',β (ylide) mechanism (eq. 2). In contrast, Hoffmann elimination, *via* pyrolysis of the quaternary ammonium hydroxide, has been shown[6] to proceed by an E2 pathway. These observations suggested to us that if such a mechanistic dichotomy were to exist, then a comparative study between $KOC(CH_3)_3$/ DMSO and the more basic dimsyl anion in DMSO may serve to identify the active base in these

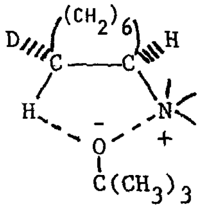


1 2 3

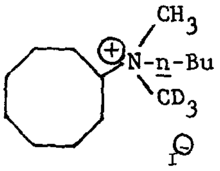
$R=CH_3$; $R'=\underline{n}$-Bu

reactions. We now report that elimination of N-n-butyl-N,N-dimethyl-cyclooctylammonium iodide (1) with $KOC(CH_3)_3$/DMSO proceeds by an E2 pathway while comparable elimination with $CH_3SOCH_2^-$/DMSO involves an α',β or ylide mechanism. We therefore suggest that the reactive base in $KOC(CH_3)_3$/DMSO is the alkoxide anion.

Our first objective was to establish what effect the different base-solvent systems had on the Z-/E-cyclooctene ratios derived from 1. Elimination of 1 in anhyd DMSO, employing 0.22 M $KOC(CH_3)_3$ at 25° gave a 20:80 Z:E ratio. Essentially identical results were obtained with inclusion of dicyclohexyl-18-crown-6 ether (0.22 M). This suggests that the potassium alkoxide is already highly dissociated in the dipolar aprotic medium. Support for this suggestion comes from the observation that elimination of 1 with $KOC(CH_3)_3$ in the nonpolar solvent benzene afforded a comparable (12:88) product ratio. Under these conditions one would also expect alkoxide ion-ammonium salt complexation[7] (4). Addition of crown ether did not alter the dominance of the higher energy (9 kcal/mol) E-cyclooctene although the proportion of the Z stereoisomer increased to 24% as a result of increased anti elimination by the free alkoxide ion. Our prior labeling studies[5] have rigorously excluded an anti elimination pathway to form the E isomer.



4



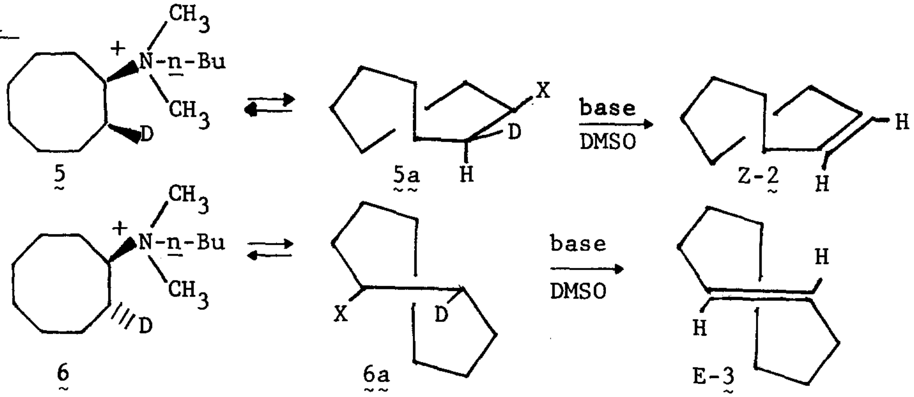
7

When NaH was employed to generate dimsyl anion in anh DMSO at 60°, subsequent addition of 1 (25°) resulted in a significantly altered Z:E ratio of 48:52. These data supported our initial supposition that different mechanisms could be in operation. We therefore sought to determine the mode of elimination in DMSO through the use of specifically deuterium labeled compounds.

The mechanisms of elimination were elucidated using essentially the same procedure as described previously.[5] N-*n*-butyl-N,N-dimethyl-*cis*-cyclooctylammonium iodide-2d$_1$ (5) and the corresponding *trans*-2d$_1$ iodide 6 were both subjected to identical reaction conditions and the reaction products (eq. 2) were purified by preparative glpc and analyzed for deuterium content by mass spectrometry (11-20 eV). Control experiments established that E-cyclooctene was not undergoing isomerization, addition or polymerization.[8]

Reaction of 5 with 0.22 M dimsyl anion in DMSO (25°) for one h gave E-3 that had retained 100% of the deuterium initially present in 5 (Table 1). The Z-cyclooctene recovered from 5 had lost 39% deuterium as a result of competitive suprafacial elimination of HX versus DX. When all antarafacial elimination can be excluded,[5] a syn k_H/k_D 1.56 may be obtained directly from these data. It is readily apparent from examination of conformer 5a that anti elimination, 5a → 2, does not result in a deuterium loss (Fig. 1).

Fig. 1



As anticipated similar experiments with the *trans*-2d$_1$ 6 gave Z-cyclooctene with 100% d$_1$ (within experimental error) with the E alkene having lost 42% deuterium. Examination of conformer 6a shows that this is consistent with a suprafacial elimination. Significantly, in both reactions the *n*-butyldimethylamine produced had incorporated all of the deuterium lost from the cyclooctyl moiety upon alkene formation excluding the intervention of an external base. Isotopic incorporation in the amine can only be accounted for by the abstraction of the more acidic α' proton by the dimsyl anion followed by an intramolecular elimination of the resulting ylide (eq. 2).

When 5 was treated with KOC(CH$_3$)$_3$/DMSO for one h at 25°, E-cyclooctene was also formed by a syn pathway as noted (Table 1) by the absence of any deuterium loss accompanying its formation. However, under these conditions the n-butyldimethylamine recovered from both 5 and 6 had failed to incorporate any deuterium excluding a ylide pathway. The data further indicate that Z-cyclooctene is formed by a competing syn and anti E2 pathway. The Z isomer obtained from 6 had lost 3% d$_1$, which upon correction for an isotope effect ($\sim$3) means that about 10% elimination occurred by the anti pathway. This loss in stereospecificity precludes direct measurement of an isotope effect but a syn k_H/k_D 3-4 may be estimated.

A syn elimination was also established for the formation of E-cyclooctene from both 5 and 6

Table 1 Elimination Reactions with Cyclooctylammonium Iodides[a]

Compound	Base/Solvent	% Z-Cyclooctene (Deuterium Content,%)	% E-Cyclooctene (Deuterium Content,%)	Amine(Deuterium Content,%)	Syn k_H/k_D
5	NaH/DMSO	45.2(61.0d_1,39.0d_0)	54.8(99.2d_1,0.8d_0)	18.4d_1,81.6d_0	1.6[b]
6	NaH/DMSO	52.6(99.5d_1, 0.5d_0)	47.4(58.2d_1, 41.8d_0)	21.9d_1,78.1d_0	1.4[c]
5	$KOC(CH_3)_3$/ DMSO	18.9(87.6d_1,12.4d_0)	81.1(99.8d_1,0.2d_0)	0.9d_1,99.1d_0	∿3-4[d]
6	$KOC(CH_3)_3$/ DMSO	19.8(97.0d_1,3.0d_0)	80.2(76.5d_1,23.5d_0)	0.4d_1,99.6d_0	3.3[c]

a) All values are corrected for the isotopic purity of the N,N-dimethylcyclooctyl amine. The accuracies of the deuterium measurements are within ± 2.0% between experiments. b) Isotope effect for formation of Z-cyclooctene. c) Isotope effect for formation of E-cyclooctene. d) After correction for anti elimination.

with $KOC(CH_3)_3$ in benzene solvent (25°, 3 h). A syn k_H/k_D of 4.0 and 3.8 was determined with and without the presence of crown ether. The Z isomer resulted from competitive syn and anti elimination with a substantial contribution from the latter pathway. All reactions in benzene proceeded by an E2 elimination with no detectable intervention of an ylide mechanism. It is worthy of note that the kinetic isotope effect for the ylide pathway, which involves a nonlinear transition state,[9] is lower that those observed under E2 conditions.

The reversibility of ylide formation[10] with dimsyl anion was established by the observation that the trideutereomethyl substrate **7** afforded tertiary amine upon elimination that had suffered a 33% reduction in d_3 content. Since control experiments have shown that labeled n-butyldimethyl-amine does not exchange hydrogen with any base-solvent system we have employed to date, the deuterium loss from **7** must occur prior to elimination.[10] No evidence for ylide formation (i.e. reduction in d_3 content) was evident when **7** was treated with $KOC(CH_3)_3$/DMSO even in the presence of crown ether.

In conclusion we have shown that active base in the elimination of a quaternary ammonium salt with $KOC(CH_3)_3$/DMSO is the alkoxide ion. We have established that a clear dichotomy in mechanistic pathway exists when either dimsyl anion or $KOC(CH_3)_3$ are employed as the base. It is also evident that one should anticipate ylide formation with relatively strong carbon and nitrogen bases while oxygen bases prefer to react by an E2 mechanism.[11]

Acknowledgement is made to the National Science Foundation (CHE 76 21992) for support of this work. RDB would also like to thank Professor J.-M. Lehn for his generous hospitality during his sabbatical leave at the University of Strasbourg where this manuscript was written.

References

1. R.A. Bartsch, Accounts Chem. Res., 8, 239 (1975).
2. C.D. Ritchie and R.E. Uschold, J. Am. Chem. Soc., 89, 2960 (1967).
3. J.I. Brauman, J.A. Bryson, D.C. Kahl and N.J. Nelson, J. Am. Chem. Soc., 92, 6679 (1970).
4. M. Szwarc, A. Streitweiser and P.C. Mowery, "Ions and Ion Pairs in Organic Reactions," M. Szwarc, Ed., Vol. II, Wiley-Interscience, New York, 1974, p. 206.
5. R.D. Bach and D. Andrzejewski, J. Am. Chem. Soc., 93, 7118 (1971).
6. J.L. Coke and M.C. Mourning, J. Am. Chem. Soc., 90, 5561 (1968).
7. J.K. Borchardt and W.H. Saunders, Jr., J. Am. Chem. Soc., 96, 3912 (1974).
8. R.D. Bach, K.W. Bair and C.L. Willis, Organometall. Chem., 77, 31 (1974).
9. W.-B. Chiao and W.H. Saunders, Jr., J. Am. Chem. Soc., 100, 2802 (1978).
10. R.D. Bach, K.W. Bair and D. Andrzejewski, Chem. Commun., 819 (1974); 820 (1974).
11. Competing E2 and ylide mechanisms were noted with MNH_2 and bicyclic compounds.

(Received in USA 19 June 1979)