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DEHYDROHALOGENATION STEREOCHEMISTRY IN SULFONYL-ACTIVATED SYSTEMS

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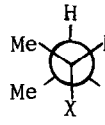
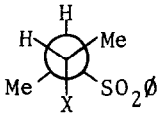
The mechanism of dehydrohalogenations and related eliminations in sulfonyl-activated systems has been of interest and controversial for many years.[1] In this communication we wish to clarify some aspects of the stereochemistry associated with these reactions with considerable emphasis on the nature of the leaving group and the significant influence exerted by it in one particular system. We have investigated sulfonyl systems 1 and 2 in detail; and in agreement with our own[2] and other studies[3] in related systems, the erythro isomers afford only E-3, the product of anti-elimination and the more stable isomer of the two possible α,β-unsaturated sulfones. Eliminations from the threo isomers (2) are more complicated in that varying amounts of E-3 and Z-3 are observed



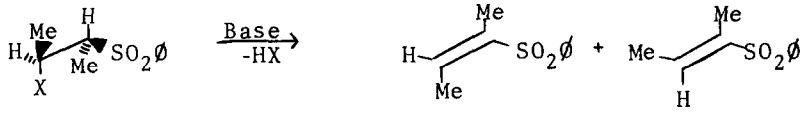
Erythro

1a X=Cl
1b X=Br



Threo

2a X=Cl
2b X=Br



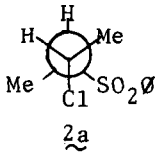
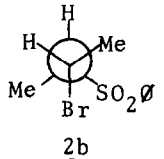
2a
2b

Z-3

E-3

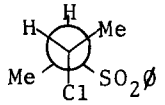
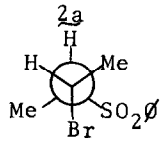
under a variety of conditions, a fact that is in disagreement with data reported[4] for 2b. Furthermore, threo isomers 2 exhibit a significant change in elimination stereochemistry as the leaving group is varied from chlorine to bromine, a variable whose significance was reported to be negligible in a closely related system.[3] A portion of our data is summarized in Table I.

Table I. Stereochemical Results in Dehydrohalogenations of Threo Isomers(2) with Amines in Benzene[5]

Compound	Base	Temperature	% Z-3 (anti elim.)	% E-3 (syn elim.)
 2a	Me_3N	27°	18%	82%
	Et_3N	81°	17%	83%
	Piperidine	81°	17%	83%
	i-Pr_2NH	81°	15%	85%
	n-$BuNH_2$	81°	21%	79%
 2b	Me_3N	27°	67%	33%
	Et_3N	81°	66%	34%
	Piperidine	81°	38%	62%
	i-Pr_2NH	81°	31%	69%
	n-$BuNH_2$	81°	33%	67%

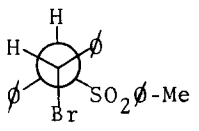
There are two additional facts about the stereochemistry of the amine reactions that we wish to stress. Increasing the steric bulk of the base, i.e., piperidine vs. diisopropyl amine, has a dramatic retarding effect on the rates but has little or no effect on the stereochemistry with either isomer. However, there is a definite temperature effect observed in eliminations involving 2b that is not observed with the corresponding chloro isomer (Table II). Clearly, lower temperatures lead to an increase in the anti-elimination component of the stereochemistry associated with the bromo isomer 2b.

Table II. Stereochemical Results as a Function of Temperature in Dehydrohalogenations of the Threo Isomers (2) With Piperidine in Benzene

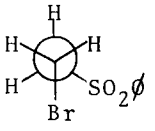
Compound	Temperature	% Z-3 (anti elim.)	% E-3 (syn elim.)
 2a	7°	21%	79%
	27°	18%	82%
	81°	17%	83%
 2b	7°	58%	42%
	27°	48%	52%
	81°	38%	62%

The simplest explanation that is consistent with this data would involve chloro isomer 2a undergoing elimination by an E1cb process, with proton removal probably being rate determining.[6] Bromo isomer 2b would have available this

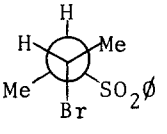
pathway as well as a competitive one (E2) with the anti-stereochemistry expected from the concerted process. In examining the sulfonyl-activated systems that have been investigated in detail, it seems clear that bromo derivatives have assumed a pivotal position in any thorough mechanistic understanding of the elimination reactions, with the available data suggesting that the elimination mechanism(s) may vary from essentially E1cb (4);[3] to the other extreme of essentially E2 (5);[6] to a competition between the two elimination modes (2b).



4



5



2b

Thus any summary of the factors that may affect the stereochemistry and mechanism(s) of eliminations in sulfonyl-activated systems must include the nature of the leaving group;[6] the strength of the base;[3] the acidifying character of substituents β to the leaving group;[3,7] and pseudo-cyclic, base-leaving group interactions.[8] It is interesting that this last factor has been suggested in lieu of a simple E1cb process to account for the large amount of syn elimination product that is observed in the reaction of 4 with amines.[3] The temperature data presented for 2b do not support this contention since low temperatures should favor pseudo-cyclic transition states and thus increase the proportion of syn elimination. Preliminary data indicate that the ionizing power of the solvent medium is another factor capable of exerting a marked influence on the stereochemistry of eliminations from 2 with polar solvent systems favoring anti eliminations.[9] We hope to report in detail on this factor in the near future.

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References

1. For example, see (a) F. G. Bordwell, J. Weinstock and T. F. Sullivan, J. Am. Chem. Soc., 93, 4728 (1971); (b) H. L. Goering, D. L. Relyea, and K. L. Howe, Ibid., 79, 2502 (1957); (c) J. Hine and O. B. Ramsay, Ibid., 84, 973 (1962). For a recent discussion of concerted and nonconcerted eliminations, see W. H. Saunders, jr., Accts. Chem. Res., 9, 19 (1976).
2. J. C. Philips, M. Aregullin, M. Oku and A. Sierra, Tetrahedron Lett., 4157 (1974).
3. V. Fiandanese, C. V. Maffeo, G. Marchese and F. Naso, J.C.S. Perkin II, 221 (1975).
4. R. Andrisano, A. S. Angeloni and A. Fini, Tetrahedron, 28, 2681 (1972).
5. The percentages of E- and Z-isomers were determined by nmr integration and are the average of at least three experiments. Control experiments with artificial mixtures indicate an accuracy of ±3% by this method. Sulfone concentrations varied from $5\text{-}8\times10^{-2}$ M, and the base concentrations in most instances were twice that of the sulfone.
6. See P. J. Thomas and C. J. M. Stirling, J.C.S. Chem. Commun., 829 (1976) and D. R. Marshall, P. J. Thomas and C. J. M. Stirling, Ibid., 940 (1975). That use of piperidine N-D affords no observable deuterium incorporation in recovered starting material (2a or 2b) provides circumstancial evidence supporting this contention.
7. S. J. Cristol and P. Pappos, J. Org. Chem., 28, 2066 (1963).
8. V. Fiandanese, G. Marchese and F. Naso, J.C.S. Chem. Commun., 250 (1972).
9. For example, reactions of 2a or 2b with amines (1°,2°,3°) in dioxane/H_2O or in anhydrous DMSO afford from 75-95% anti elimination.