Tetrahedron Letters No.25, pp. 2955-2958, 1968. Pergamon Press. Printed in Great Britain.

SITE SELECTIVITY AND STEREOSPECIFICITY IN MASS SPECTRAL ELIMINATION REACTIONS

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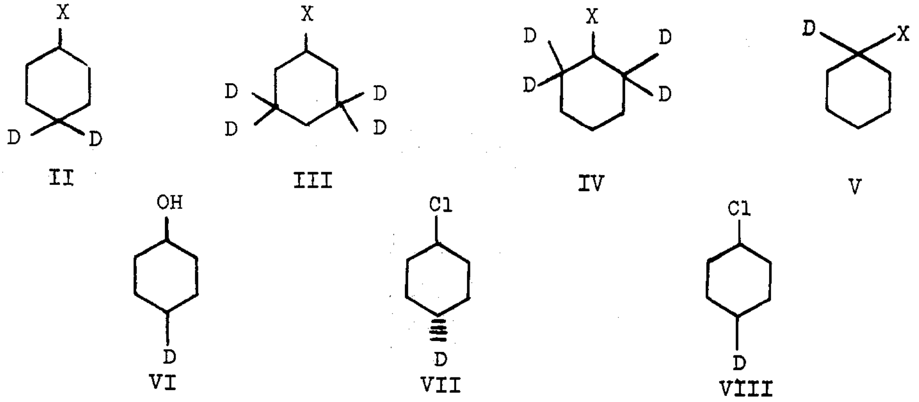
(Received in USA 15 January 1968; received in UK for publication 22 March 1968)

Detailed studies have shown that the electron impact induced loss of water from acyclic alcohols (1) proceeds by abstraction of a C-4 hydrogen to the extent of 90% while results on acyclic chlorides (2) show that the loss of hydrogen chloride proceeds predominantly ($>$ 70%) by abstraction of a C-3 hydrogen. Following the behavior of primary acyclic alcohols, although with less specificity, cyclohexanol has been found to eliminate water preferentially by a 1,4 process (3). The site selectivity for cyclohexyl chloride would be of interest to determine if the divergence in the linear molecules carries over to the cyclic case. We have prepared deuterated samples of cyclohexanol (I, X=OH) and cyclohexyl chloride (I, X=Cl) in order to directly compare the chloride and alcohol site selectivity.

Scheme 1 shows the compounds prepared for this study.

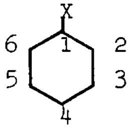
Scheme 2 presents our findings on the hydrogen abstraction sites for elimination of water and hydrogen chloride from compounds II, III, IV, and V (X=OH,Cl).

SCHEME 1[a,b]



a. X=Cl or OH. The chlorides (except for VIII) were prepared from the alcohols with phosphorus pentachloride. b. II and III were prepared from the monoethylene ketal of 1,4 cyclohexanedione (4) by simple steps. IV and V were prepared by reduction of the appropriate cyclohexanone. VIII is made by lithium aluminum deuteride reduction of the tosylate of trans-4-chlorocyclohexanol (5). VI arises by similar treatment of the monotosylate of trans-1,4 cyclohexanediol (6). In all cases the deuterium incorporation was close to 100%.

SCHEME 2



$\rightarrow [C_6H_{11}X]^{\cdot+} \longrightarrow HX + [C_6H_{10}]^{\cdot+}$

	% H abstraction site			
X	1	2(6)	3(5)	4
OH	0	<6	41	55
Cl	0	0	44	46

The data in Scheme 2 show that the loss of water from I (X=OH) (7) arises predominantly by abstraction of a C-4 hydrogen with a substantial proportion also coming from C-(3)(5). The proportion of C-4:C-3 loss, after correction for the statistical excess of C-(3)(5) hydrogens, is 73:27. Similarly, the C-4:C-3 proportion for hydrogen chloride loss from I(X=Cl) is 68:32. It can therefore be seen, in striking contrast to the acyclic molecules, that the cyclohexyl derivatives exhibit very similar site selectivities. A possible factor, excluded for the acyclic cases, in the site selectivity of cyclohexyl compounds is for elimination of HX to be preceeded by α-cleavage (8). The mass spectral behavior of compounds VI, VII and VIII were examined in order to gauge the extent of an α-cleavage mechanism.

Table I presents the hydrogen abstraction data for loss of water and hydrogen chloride from VI, VII and VIII, and the calculated cis:trans proportions for the elimination.

Table I

A = Percent Deuterium Abstraction from C-4
B = Percent (cis:trans) elimination from C-4
C = B corrected for lack of specificity in formation of VI

	A	B	C
VI	44	70:30	80:20
VII	7	88:12	100:0
VIII	46	100:0	100:0

First, it is apparent that the elimination of the C-4 hydrogen is attended by a considerable degree of stereospecificity. Since the displacement of tosylate by lithium aluminum hydride is known to occur with inversion of configuration (9), and since VI derives from the monotosylate of trans-1,4 cyclohexanediol (6), the data in Table I demonstrate, assuming complete specificity of the deuteride reduction (see below), that 70% of the 1,4 eliminations in VI occur via abstraction of the cis C-4 deuterium (10). Since VI was converted to VII with phosphorus pentachloride, a process which is known to involve stereospecific inversion of configuration (12), it follows that the 1,4 elimination of hydrogen chloride involves abstraction of a C-4 cis hydrogen and that the stereospecificity for 1,4 elimination from I (X=OH) is somewhat lower than that from I (X=Cl). Indeed, the data for VIII show that the stereospecificity for the lithium aluminum deuteride reduction of the monotosylate of trans-1,4 cyclohexanediol is lower than that from the tosylate of trans-4-chlorocyclohexanol and further that the 1,4 elimination reaction in cyclohexyl chloride is stereospecific. After correction for the presence of trans-4-deuterocyclohexanol in VI the results (Table I(C)) show that while the ring is substantially intact in cyclohexanol it has complete integrity in cyclohexyl chloride (8).

The findings of strong ligand dependency on the site selectivity of alkyl chlorides and retention of gross ground state structure for the parent ion (i.e. the ring is intact) suggest that this ubiquitous mass spectral reaction may be well suited for use in a structure reactivity (selectivity in this case) study. Such a study is needed to test the application of ground state structural parameters (e.g. size of groups) to ionized state processes (13).

In addition these results lend support to the connection between onium ion formation and site selectivity (14) since the formation of the cyclic onium ions is restricted to primary acyclic systems.

Acknowledgement: This work was supported by the Petroleum Research Fund of the American Chemical Society (Grant No. 1104-G1) and by a grant from the Horace H. Rackham School of Graduate Studies at the University of Michigan.

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   (b) Prolonged treatment of 7-oxa-bicyclo-[2,2,1]-heptane, the expected assistance product, with lithium aluminum hydride even with excess aluminum chloride leads to only traces of cyclohexanol. See: E. L. Allred and S. Winstein, J. Amer. Chem. Soc., 89, 4008 (1967).

7. (a) III shows loss of DHO (32%) and D_2O (9%).
   (b) These results are in qualitative agreement with earlier studies on cyclohexanol (3). Our measurements were made on a CEC(103C) mass spectrometer at 70 ev with a room temperature inlet and the ion source at 125°C. We have observed a significant temperature effect on the site selectivities which bring the present results and the previous work (3b) in closer accord. We shall report later on the details of this observation. (We thank Dr. A. Duffield of Stanford University for the variable temperature spectra.)

8. Ample precedent exists for this cleavage in alcohols while little evidence can be found for it in chlorides. See: H. Budzikiewicz, C. Djerassi and D. H. Williams, Mass Spectrometry of Organic Compounds, Holden-Day, Inc., San Francisco, 1967, Ch. 2 and 12.

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10. Previous mass spectral work on the cis and trans isomers of 1,4 cyclohexandiol (3a) and 4-t-butylcyclohexanol (11) show that the trans isomers lose larger amounts of water in both cases. The diol (3a) was studied by deuterium labelling and the C-4 hydrogen was shown to be involved. This work strongly suggests that the rings are substantially intact although some trans-deutrium is lost in 1,4 dideutero-1, 4-cis-cyclohexanediol (3a).

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