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STEREOCHEMISTRY OF ALLYLIC NUCLEOPHILIC DISPLACEMENT PROCESSES BY THE ORBITAL DISTORTION TECHNIQUE

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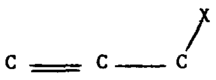
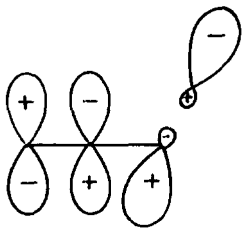
Although nucleophilic allylic displacement reactions have been well documented in the literature, a serious question remains as to the detailed mechanism of such reactions. Is the reaction truly concerted or stepwise? Bordwell[1] has concluded that "there appear to be no unambiguous examples of SN_2' concerted mechanisms." Based upon the work of Stork and White,[2] the stereochemistry of allylic displacement reactions has been generally accepted to be one in which the nucleophile approaches cis to the leaving group. Some recent work by Rickborn[3] and Johnson[4] on the reaction of lithium dimethylcuprate with 1,3-cyclohexadiene monoepoxide, however, appears to produce stereochemical results in contradiction to those of Stork and White. Thus, while it has been well established that in direct displacements (SN_2) attack of the nucleophile occurs from the backside of the carbon bearing the leaving group, the stereochemistry of allylic displacements appears to be still in question. This communication reports a unified picture of the above reactions using the orbital distortion technique discussed in the previous communication.[5]

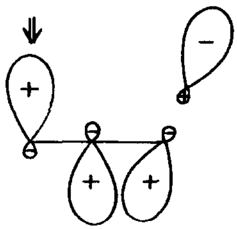
In general terms, let us consider a leaving group X located in an allylic position (I). In an allylic nucleophilic displacement reaction (attack at C_3), the most probable direction of



I

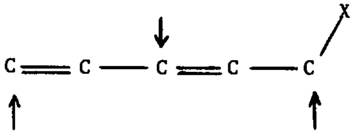


II



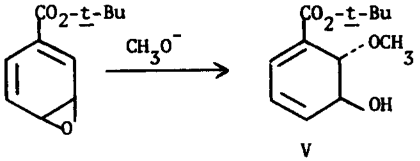
III

nucleophilic approach is governed by the LUMO of the substrate. In this example, it is the C-X substituent in the 1-position which is primarily responsible for the distortion of the π-system. Figure II represents the nodal properties of the undistorted π-system mixed with the C-X sigma bond and Figure III shows the distortion of the system about the nodal plane after minimizing antibonding and maximizing bonding. The results clearly indicate that the most probable direction of attack is *cis* to the leaving group in accord with the experimental results of Stork and White.[2] Figure III also indicated that the stereochemistry of attack at C-1 is from the backside in agreement with a host of data.[6] In general, one may conclude from this analysis that vinyllogs of allyl system I would be attached by nucleophiles in an alternating manner as shown in IV.

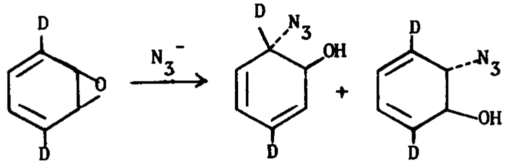


IV

Indeed, Berchtold et al.[7,8] report that reaction of 4-carbo-*tert*-butoxybenzene oxide with methoxide ion affords V and reaction of benzene oxide-3,6-d_2 with azide ion produces VI and VII. The formation of V and VII may be formally regarded as a diallylic nucleophilic displacement process and the observed *trans* stereochemistry of these products coincide with the predictions of the orbital distortion technique.[9]

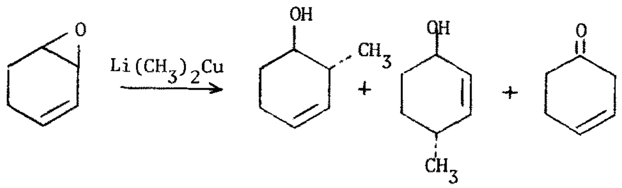


V



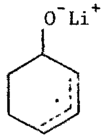
VII VI

The work of Rickborn[3] and Johnson[4] may be summarized by eq. 1 where the formation of X appears formally to be an allylic displacement process. House[11] has provided some evidence that lithium dialkylcuprate reactions with enone systems proceed *via* a single electron transfer step followed by transfer of an alkyl group. It is not unreasonable, therefore, to assume that the

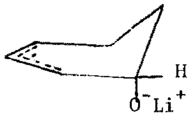


X

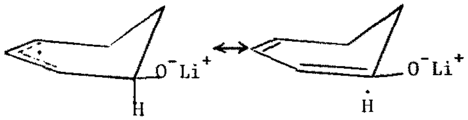
first step involves electron-transfer to X to form intermediate XI. This, of course, would be greatly facilitiated by the coordination of lithium ion with oxygen. Intermediate XI may assume



XI

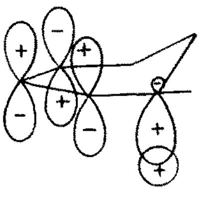


XII

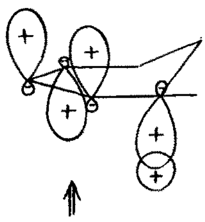


XIII

two possible conformations XII and XIII. From a steric point of view XIII would be expected to be more stable than XII since the bulky solvated $-O^{\ominus}Li^{\oplus}$ group occupies the less encumbered pseudo-equatorial position. Electronic arguments would also favor XIII since hyperconjugative structure XIV would be stabilized by the presence of $-O^{\ominus}Li^{\oplus}$. It may be concluded that it is the pseudo-axial C-H in the 1-position of XIII which is primarily responsible for the distortion of the π-system about the nodal plane. The pseudo-axial C-H in the 5-position also occupies a favorable geometry for interaction with the π-system but the magnitude of such interaction should be small compared to that of the C-H in the 1-position because of hyperconjugative structure XIV. Figure XV represents the nodal properties of the undistorted π-system and C-H sigma bond and Figure XVI shows the distortion of the system about the nodal plane. The conclusion is



XIV



XV

that the alkyl group would attach C-4 so as to product the *trans*-product in accord with the experimental results.[12]

In summary, (1) the orbital distortion technique predicts that allylic nucleophilic displacement reactions occur with a *cis*-stereochemistry and (2) the apparent inconsistency between the work of Stork[2] and Rickborn[3] and Johnson[4] has been eliminated.

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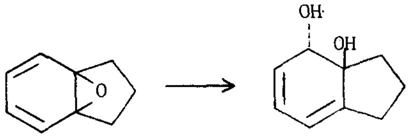
9. It is interesting to note that indane 8,9-oxide transformed to VIII by microsomal epoxide hydrase may be considered to also represent a diallylic nucleophilic displacement process although other equally attractive mechanisms have been suggested.[10]



10. T. C. Bruice, D. M. Jerina et al., J. Amer. Chem. Soc., 95, 6041 (1973).
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12. It is assumed that the *trans*-2-methylcyclohex-3-ene-1-ol product arises from direct attack on the epoxide ring by an ionic mechanism.