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THE STEREOCHEMISTRY OF THE PREPARATION AND CUPROUS CHLORIDE-CATALYZED REARRANGEMENT OF A PROPARGYL CHLORIDE

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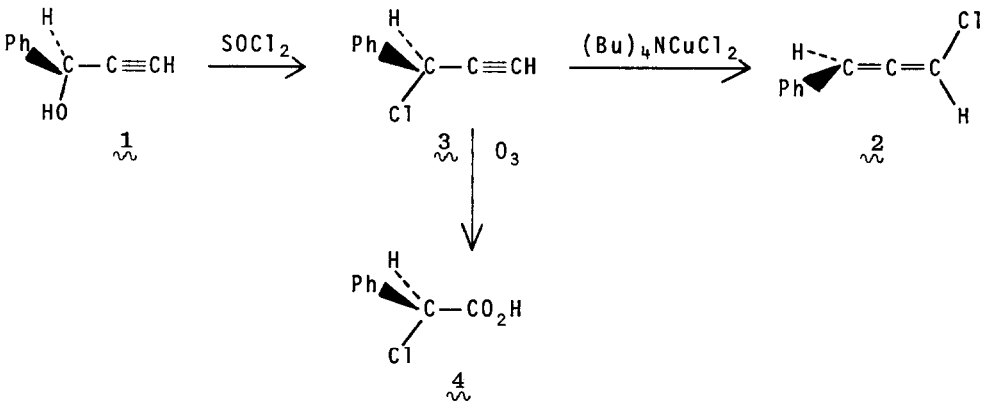
Conversions of propargyl alcohols to allenyl halides, either directly or through the corresponding propargyl halides, have been used extensively in allene synthesis.[1] Unfortunately, despite the potential for assymmetric synthesis of chiral allenes, the stereochemistry of these reactions has been neglected, with a few exceptions.[2-5] In particular, nothing has been reported concerning the stereochemistry of the cuprous halide-catalyzed rearrangement of propargyl halides. As part of a study of the mechanism of this reaction, we have investigated the stereochemistry of the conversion of 1-phenyl-2-propyn-1-ol (1) to 1-chloro-3-phenyl-1,2-propadiene (2) *via* the cuprous chloride-catalyzed rearrangement of 3-chloro-3-phenyl-1-propyne (3).



1 3 2 4

Alcohol 1 was partially resolved according to the procedure of Iwai and Tomita,[6] and obtained as the R-(-) enantiomer, with an optical purity of 81%.[7] Addition of thionyl chloride in anhydrous ethyl ether to 1 at 0°, followed by reaction at room temperature for two hours gave 3 in 67% yield, $[\alpha]_D^{25}$ -9.8° (c 25, C_6H_6). This material was obtained essentially pure, and free of the corresponding allenyl chloride 2, as shown by the absence of the typical C=C=C stretch absorption at 1950 cm^{-1} in the IR spectrum of the product.[8]

The optical purity and absolute configuration of 2 were determined by ozonolysis of a portion, which gave (S)-(+)-1-chloro-1-phenylacetic acid (4) in 27% yield, $[\alpha]_D^{25}$ +35° (c 0.43, C_6H_6), 18% optically pure.[9] Thus, 3 must have the R configuration, as shown, and was formed by substitution with 22% net retention. This stereoselectivity is less than that usually obtained from reaction of thionyl chloride with chiral alcohols under S_Ni conditions,[10] and is probably due to the relative stability of the highly delocalized phenyl-substituted propargyl cation of the ion-pair which presumably results from decomposition of an intermediate chlorosulfite ester.

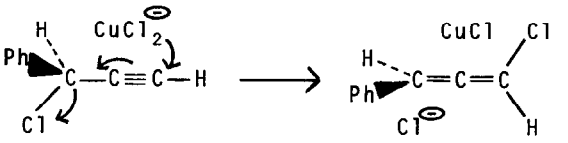
Rearrangement of 3 was effected by treatment at room temperature for 24 hours with cuprous chloride solubilized in dry acetone by tetrabutylammonium chloride, a reagent similar to those reported by Gaudemar.[11,12] Allenyl chloride 2 was obtained free of substantial propargyl isomer in 62% yield, $[\alpha]_D^{25}$ -94° (c 0.9, $CHCl_3$).

Application of Lowe's Rule[13] predicts that the (-) enantiomer of 2 should have the R configuration, as shown. On this basis, the predominant orientation of rearrangement would be such that the entering chloride is anti to that of the departing chloride. The degree of this stereoselectivity may be estimated through use of Brewster's helix model of optical activity in allenes,[14] by which a maximum specific rotation for (R)-2 in chloroform can be predicted to be approximately -418°, giving an estimated optical purity of 22%, a figure that is too high, since the optical purity of 3 was only 18%.

It should be emphasized that caution must be exercised when predicting

configuration based upon sign of rotation and empirical correlations alone. One example,[4] particularly, seems to indicate that two allenyl halides, differing only in the nature of the halogen, can have rotations of opposite sign although they have the same configuration, contrary to Lowe's Rule. Although this conclusion might be questioned on the basis of the very low yields and specific rotations obtained for the compounds used in that correlation, it is clear that the configuration of 2 must remain in some doubt. However, the magnitude of its specific rotation does indicate that the stereoselectivity of the rearrangement producing it is likely to be fairly high.

Since a preliminary kinetic study indicates a kinetic order of one for cuprous chloride in this reaction,[15] one possible mechanism for this reaction may be formulated as below, assuming the inferred stereochemistry to be correct. Further kinetic and stereochemical studies are expected to help further clarify the mechanism of this reaction.



The anti attack proposed here is contrary to the usual representation of this rearrangement, in which syn attack by CuCl has been assumed,[16] an orientation which appears to have been eliminated for the system reported here. Since this rearrangement involves what is essentially an S_N2' mechanism, it is of interest that such reactions in acyclic allylic systems have shown stereochemistry predominantly (or exclusively) syn when the attacking nucleophile was neutral (diethylamine),[17] and anti when the nucleophile was negative (thiolate).[18] The latter situation would seem to apply here and we do, indeed, observe anti attack. In this regard, it may be relevant that anti attack was also reported to predominate in the reaction of lithium dimethylcuprate with a chiral propargyl acetate to form a methyl-substituted allene.[19]

ACKNOWLEDGMENT

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