Tetrahedron Letters No.5, pp. 321-324, 1965. Pergamon Press Ltd.
Printed in Great Britain.

CARBENOID REACTIONS WITH IMINES

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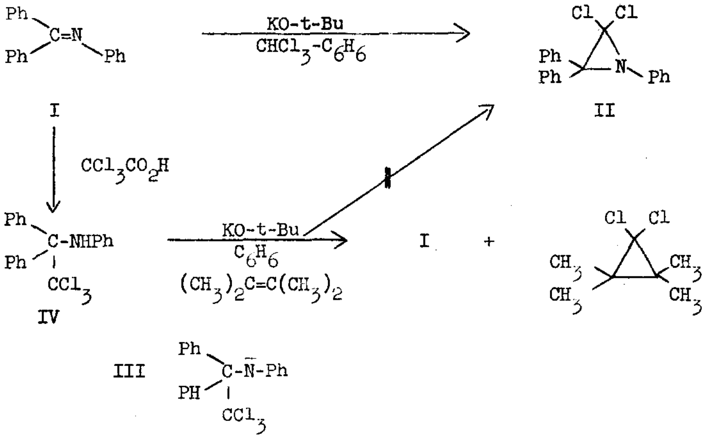
(Received 8 December 1964)

Questions have recently been raised concerning the general mechanism of carbenoid reactions(1) and specifically the importance of halocarbene intermediates.(2) As a consequence of our search for general routes to haloaziridines, we have had occasion to make frequent use of carbenoid additions to imines. From this work we have obtained evidence which is pertinent to the role of potential noncarbene intermediates.

The ability of the heteroatom to accept negative charge in imines which lack α-hydrogens, as with the analogous ketones, facilitates attack by a variety of nucleophiles.(3) Especially instructive is the nucleophilic attack by diazomethane on imines followed, in a second step, by ring closure to a triazoline.(4) By contrast, diazo compounds react with alkenes *via* concerted 1,3-dipolar addition.(5) From the above considerations, it seemed necessary to consider the possibility that carbenoid conversion of imines to haloaziridines takes place by means of initial nucleophilic attack by the halomethane anion with subsequent ring-closing elimination of halide ion. The following experimental evidence, however, argues strongly against such a route.

Benzophenone anil (I) was converted to 1,2,2-triphenyl-3,3-dichloroaziridine, m.p. 95.5-96.0° (II) by the reaction of potassium *t*-butoxide with chloroform at room temperature.(6) In order to learn whether the anion, III, is an intermediate in the formation of II, III was generated in an alternative manner. Treatment of IV(7) with potassium *t*-butoxide(8) in benzene (under identical conditions to the synthesis of II) yielded approximately 75% I and 25% II. A clue as to the origin of II was found by repeating the reaction in the presence of excess tetramethylethylene. Under these conditions, no detectable (i.e., less than 5%) aziridine was produced. It seems clear, therefore, that developing negative charge on nitrogen is dissipated by elimination of trichloromethyl anion and not by ring closure.(9)



Although gem-dihaloaziridines have been known for some time, no monochloroaziridines have previously been reported.(11) Köbrich has reported that at stable reagent, $LiCHCl_2$, may be prepared from butyllithium and methylene chloride at -110°.(13) Addition of N-benzylideneaniline in ether to excess $LiCHCl_2$ at temperatures below -70° produced a homogeneous orange solution which was allowed to warm to room temperature slowly. Work-up gave a high yield of crude material.* Inspection of the n.m.r. spectrum of this material revealed doublets (J = 5 c.p.s.) centered at 3.12 and 4.33 p.p.m. (in addition to complex phenyl absorbtion). The absence of other absorbtion which could possibly be attributed to the other isomer indicates the exclu-

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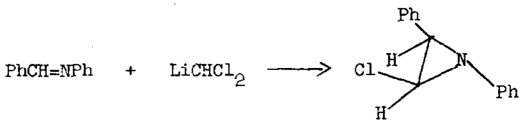
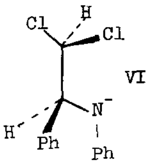
* Satisfactory analyses have been obtained for all new compounds with the exception of this monohaloaziridine which was too reactive to allow purification for analysis. The structure of this compound is supported by spectral data as well as by conversion to suitable analyzable derivatives. A wide variety of chemical behavior might be expected from a reactive, difunctional molecule of this type. We shall soon report on the chemistry and synthetic utility of this and related monohaloaziridines including additional structural and stereochemical information.

sive course of the reaction and the magnitude of the coupling constant(14) (as well as other evidence) demonstrates that this reaction stereoselectively yields the cis isomer (V).(15)

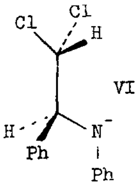


V

To rationalize this observed stereochemistry in terms of initial nucleophilic attack, it is necessary to assume that ring closure occurs from conformation VI. There is no compelling reason, however, to expect this con-



VI



VII

formation to be the sole or predominant product. To the extent that time exists for rotation about the relevant single bond, cyclization from conformation VII should also become possible and probably predominate. The above stereochemical result can be rationalized in terms of a transition state favored by attraction between the electron pair on nitrogen and the partially positive charged chlorine of the monochlorocarbene species.(17) By contrast, it seems difficult to account for the high observed stereoselectivity by the recently proposed mechanism involving nucleophilic attack by olefin of the trichloromethyl anion.(2)

ACKNOWLEDGMENT

We should like to thank Professor J. O. Edwards for his interest and helpful discussions and M. Wojcik and H. Frohofer for valuable assistance.

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(6) Procedure of A. G. Cook and E. K. Fields, J. Org. Chem. 27, 3686 (1962).

(7) Prepared by refluxing toluene containing I and trichloroacetic acid for three hours, m.p. 122.5-123.0. Procedure of A. Lukasiewicz, Tetrahedron 20, 1 (1964).

(8) The triphenyl system was chosen to avoid ambiguity of proton abstraction at this point.

(9) It is probable that this elimination is a two-step process.(10) It should be pointed out, however, that concerted routes can be written from IV to both I and II.

(10) D. V. Banthorpe, *Elimination Reactions*, Elsevier Publishing Co., New York, N. Y., 1963, p. 84.

(11) Application of Closs's procedure(12) for the generation of monochlorocarbene yielded only adducts of alkyllithium to the imine.

(12) G. L. Closs and L. E. Closs, J. Am. Chem. Soc. 82, 5723 (1960).

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(14) S. J. Brois, J. Org. Chem. 27, 3532 (1962); A. Hassner and C. C. Heathcock, Tetrahedron Letters 1125 (1964).

(15) Köbrich(13) has also stated that $LiCHCl_2$ reacts with benzophenone to give the product of nucleophilic addition to the carbonyl group. No mention was made of the cyclization product, a chloroepoxide, or its rearrangement products.(16) In view of the greater reactivity of ketones towards nucleophilic attack, this result seems to point out a fundamental difference between nucleophilic attack and ring-forming mechanisms.

(16) R. N. McDonald and P. A. Schwab, J. Am. Chem. Soc. 85, 4004 (1963).

(17) J. Hine, *Divalent Carbon*, The Ronald Press Co., New York, N. Y., 1964, p. 65.