Tetrahedron Letters No. 11, pp. 485-488, 1962. Pergamon Press Ltd. Printed in Great Britain.

A NOVEL REARRANGEMENT OF AN AMINOÖXY COMPOUND

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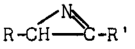
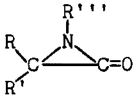
(Received 11 April 1962)

A SIZEABLE body of evidence has now accumulated suggesting that a number of rearrangement reactions proceed via three-membered nitrogen-containing rings. For example, the Neber rearrangement of ketoxime tosylates,[1] the rearrangement of N,N-dichloro-sec-alkylamines,[2-4] and the synthesis of α-amino ketones and acids from N-chloroketimines[5] have in common the azirine intermediate A (or some closely related aziridine derivative).



A



B

More recently, reports[6,7] of the transitory formation of aziridinones (α-lactams, B) in the Favorskii-type rearrangement of α-chloroamides have appeared in the literature. The intermediates A and B are presumably formed via the nucleophilic displacement of the leaving group on nitrogen (tosylate or halogen) by a neighboring carbanion.

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[1] D.J. Cram and M.J. Hatch, *J. Amer. Chem. Soc.* **75**, 33, 38 (1955).

[2] H.E. Baumgarten and F.A. Bower, *J. Amer. Chem. Soc.* **76**, 4561 (1954).

[3] H.E. Baumgarten and J.M. Petersen, *J. Amer. Chem. Soc.* **82**, 459 (1960).

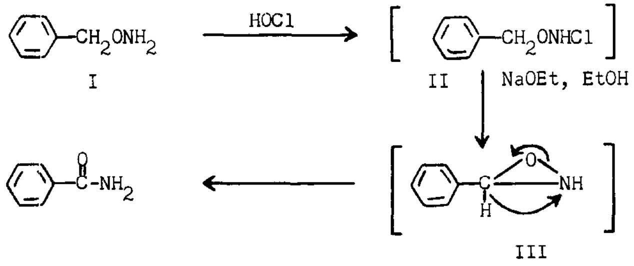
[4] G.H. Alt and W.S. Knowles, *J. Org. Chem.* **25**, 2047 (1960).

[5] H.E. Baumgarten, J.E. Dirks, J.M. Petersen and D.C. Wolf, *J. Amer. Chem. Soc.* **82**, 4422 (1960).

[6] H.E. Baumgarten, R.L. Zey and U. Krolls, *J. Amer. Chem. Soc.* **83**, 4469 (1961).

[7] S. Sarel and H. Leader, *J. Amer. Chem. Soc.* **82**, 4752 (1960); see also J.C. Sheehan and J. Frankenfeld, *Ibid.* **83**, 4792 (1962).

As part of a general program dealing with hydroxylamine chemistry,[8] we became interested in determining if this type of intramolecular nucleophilic displacement could occur in a suitably constructed aminoöxy compound to give an oxazirane[9] intermediate. The present communication presents evidence that in the case of O-benzylhydroxylamine (I)[10] this indeed does occur. Monochlorination of I with one equivalent of aqueous hypochlorous acid[11] afforded the N-chloro aminoöxy derivative (II)[12] which, without purification, was added to a refluxing solution of excess sodium ethoxide in ethanol. Distillation (pot. temp. 190°) of the crude intermediate induced further (thermal) rearrangement to give a 20 per cent yield (based on recovered I) of benzamide, m.p. 123-124.5.[13] This result may be rationalized



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[8] This paper may be considered Hydroxylamine Chemistry. III. For Part II, cf. L.A. Paquette, J. Org. Chem. 27, in press (1962).

[9] For an excellent study of the classical preparation and properties of the oxaziranes see W.D. Emmons, J. Amer. Chem. Soc. 79, 5739 (1957).

[10a] R. Behrend and K. Leucks, Liebigs Ann. 257, 206 (1890); [b] E.L. Schumann and R.V. Heinzelman, J. Med. Pharm. Chem. to be published.

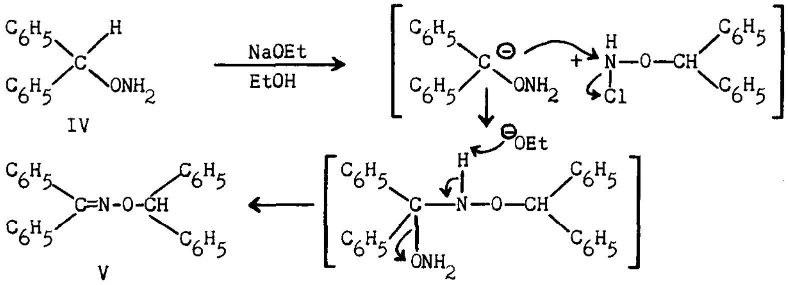
[11] Prepared by making commercial hypochlorite solution slightly basic with sodium hydroxide solution.

[12] Based on the sizeable quantities of I recovered after this reaction sequence, one can conclude that the N-chlorination does not proceed to a great extent, probably because the O-substituted hydroxylamines are somewhat less basic than primary alkylamines. Attempts to use t-butylhypochlorite as the chlorinating agent [see W.E. Bachmann, M.P. Cava and A.S. Dreiding, J. Amer. Chem. Soc. 76, 5554 (1954)] were unsuccessful because this reagent exploded when added to a cold ethereal solution of I.

[13] The assignment of structure was based upon a comparison of the product from the present synthesis with an authentic sample with respect to melting points and infrared spectra.

by assuming that an intermediate is formed in which the nitrogen of the original aminoöxy compound is bonded to the benzylic carbon atom, and is evidence for the formation of the oxazirane III which subsequently rearranges to benzamide at the elevated temperature.[9]

Because of the increased acidity of the alpha-hydrogen of benzhydryl- (as compared to benzyl) groups, O-benzhydroxylamine (IV)[10b] was similarly subjected to the monochlorination and base treatment reactions to determine if a mechanistically similar course would be followed. Distillation of the product afforded a 15 per cent yield of benzhydrol;[14] from the undistilled material was obtained a 41 per cent yield of O-benzhydrylbenzophenone oxime (V).[15] Structure V was further confirmed by its unequivocal synthesis from O-benzhydrylhydroxylamine and benzophenone.



It is reasonable that, again in the case of IV, complete conversion to the N-chloro derivative does not occur. It might then be argued that, in the presence of ethoxide ion, IV is converted to its anion which displaces the halogen atom of the N-chloro intermediate.[16] The resulting

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[14] The formation of benzhydrol may be explained by the attack of ethoxide ion on the nitrogen atom of IV to eliminate benzhydroxide ion; see R. Brown and W.E. Jones, J. Chem. Soc. 781 (1946).

[15] A.C. Cope and A.C. Haven, Jr, J. Amer. Chem. Soc. 72, 4896 (1950).

[16] A similar type of mechanism has recently been suggested for the conversion of benzhydryl chloride to tetraphenylethylene in the presence of dipotassio succinimide: D.R. Bryant and C.R. Hauser, J. Amer. Chem. Soc. 83, 3468 (1961).

product subsecuently can undergo base-catalyzed elimination of hydroxylamine to give V. Alternative mechanisms can also be considered, but in the absence of more detailed information exhaustive enumeration of these would be pointless.[17]

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[17] Another possibility worthy of mention because it resorts to a similar oxazirane intermediate is: