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THE REARRANGEMENT OF AROMATIC ALDOXIMES ON REDUCTION WITH LITHIUM ALUMINUM DEUTERIDE AND LITHIUM ALUMINUM HYDRIDE

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Although the rearrangement which occurs on reduction of aromatic ketoximes with lithium aluminum hydride (equation 1a) is well known,[1,2] the reductive rearrangement of aromatic aldoximes under similar conditions (equation 1b) has not been reported, despite the fact that a number of aldoximes have been reduced by this method.[3] We wish to make a preliminary report of some results observed on the reduction of several aromatic aldoximes with lithium aluminum deuteride and lithium aluminum hydride, wherein such a rearrangement occurred.

$$\underset{\text{NOH}}{\underset{\|}{\text{ArCR}}} \xrightarrow{\text{LiAlH}_4} \underset{\text{NH}_2}{\underset{|}{\text{ArCHR}}} + \text{ArNHCH}_2\text{R} \qquad (1)$$

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a, R = alkyl
b, R = H

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[1] N. G. Gaylord, Reduction With Complex Metal Hydrides, p. 756. Interscience, New York (1956).

[2] R. E. Lyle and H. J. Troscianiec, J. Org. Chem. 20, 1757 (1955).

[3] Reference 1, pp. 751-752.

The reduction of aromatic aldoximes with lithium aluminum deuteride was prompted by recent observations[4] which suggested that the reductive rearrangement of ketoximes proceeds non-stereospecifically. This conclusion was based on the fact that the two geometrical isomers of isobutyrophenone oxime (Ia, Ar=Ph, R=i-Pr) underwent rearrangement very readily on reduction with lithium aluminum hydride to give comparable yields (about 70%) of N-isobutylaniline. It was shown experimentally that isomerization of the oximes did not occur under the conditions of the reaction.

The apparent non-stereospecificity of the reductive rearrangement coupled with the fact that aldoximes, when undergoing the Beckmann rearrangement, are usually transformed only to the unsubstituted amides and seldom to the substituted formamides (presumably because of preliminary isomerization of the oximes before rearrangement)[5], suggested that the failure of aldoximes to undergo reductive rearrangement with lithium aluminum hydride might also have been due to a non-stereospecific reaction in which a preferential hydride shift occurred.

To test this hypothesis, acetophenone oxime (for reference purposes) and the two stereoisomers of benzaldoxime[6] were reduced with lithium aluminum deuteride under conditions analogous to those used in the lithium aluminum hydride reactions.[2,4] Acetophenone oxime (equation 2a, Ar=Ph, R=CH_3) gave a mixture of 62% 1-phenyl-1-deuterioethylamine (IVa, Ar=Ph, R=CH_3) and 38% N-(1,1-dideuterioethyl)-aniline (Va, Ar=Ph, R=CH_3) with no

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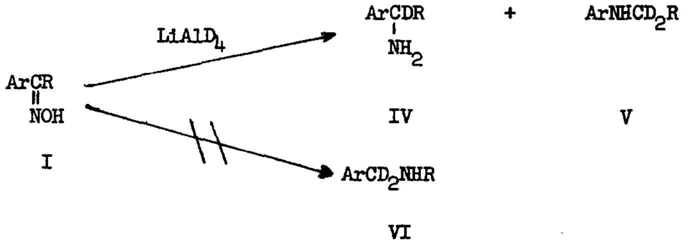
[4] A. E. Petrarca, Ph.D. Thesis, University of New Hampshire (1959); Diss. Abstr. 20, 1178 (1959).

[5] L. G. Donaruma and W. Z. Heldt, Organic Reactions Vol. 11, pp. 41-42. John Wiley, New York (1959).

[6] Anti-benzaldoxime, m.p. 115-117°, was prepared by the isomerization of syn-benzaldoxime (Eastman), m.p. 35°, according to the procedure of O. L. Brady and F. R. Dunn, J. Chem. Soc. 123, 1783 (1923); other oximes were prepared by standard procedures described in the literature.

evidence of hydrogen-deuterium exchange at the carbon-deuterium bond even when hydrolysis was effected with ordinary water instead of deuterium oxide during work-up of the reaction mixture. According to these results, a hydride shift in the corresponding reduction of the benzaldoxime isomers (equation 2b, Ar=Ph) should have resulted in the formation of α,α-dideuteriobenzylamine (VIb, Ar=Ph). Although none of this product was formed, both *syn*- and *anti*-benzaldoxime gave product mixtures containing about 97% α-deuteriobenzylamine (IVb, Ar=Ph) and 3% *N*-dideuteriomethylaniline (Vb, Ar=Ph). There was no evidence of isomerization of unreacted oxime in each case, as determined by spectral data.



(2)

a, R = alkyl
b, R = H

The somewhat unexpected formation of N-dideuteriomethylaniline prompted us to check the reduction of *syn*-benzaldoxime with lithium aluminum hydride (equation 1b, Ar=Ph). Sure enough, a mixture containing the expected benzylamine and a small amount of *N*-methylaniline was obtained. However, since electron releasing substituents were found to promote the migration of aroyl groups in the reductive rearrangement of *para*-substituted acetophenone oximes,[2,4] the above results were checked further by carrying out the reduction of *p*-anisaldoxime (Ib, Ar=*p*-$CH_3OC_6H_4$), m.p. 57-59°,[7] with lithium aluminum hydride

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[7] According to E. L. Skau and B. Saxton, *J. Phys. Chem.* **37**, 197 (1933), p-anisaldoxime of this melting point represents a mixture of the *syn* and *anti*-isomers. No attempt was made to obtain one or the other of the pure isomers.

and lithium aluminum deuteride. As expected, a much higher percentage (31%) of the rearrangement product (IIIb or Vb, Ar=p-$CH_3OC_6H_4$) was obtained from this oxime.

Thus, although the experimental results preclude the possibility of a hydride shift in the reduction of aromatic aldoximes with lithium aluminum hydride (or deuteride), they clearly show that reductive rearrangement, which had previously been reported to occur only with aromatic ketoximes, and in one instance with an aliphatic ketoxime[8], also occurs with aromatic aldoximes. The results also tend to substantiate the non-stereospecificity of the reductive rearrangement since, as was observed in the reduction of the isobutyrophenone oxime isomers, the product mixtures obtained from syn- and anti-benzaldoxime were essentially the same, with no evidence of oxime isomerization under the reaction conditions.

Experimentally, the mixtures of amines obtained from these reactions were separated by a method previously described.[4,9] All non-deuterated products, except N-methyl-p-anisidine (IIIb, Ar=p-$CH_3OC_6H_4$), were characterized by the identity of their infrared and mass spectra with those of authentic samples. N-Methyl-p-anisidine was characterized by physical constants (m.p. 35-37°, reported[10] m.p. 37°; hydrochloride m.p. 117-120°, reported[10] m.p. 119°) as well as by its infrared and mass spectra. All deuterated products were characterized by infrared and n.m.r. spectra and by a comparison of their mass spectral patterns with those of the corresponding non-deuterated compounds. After characterization of the reaction products, the compositions

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[8] A. T. Blomquist, B. F. Hallam, and A. D. Josey, J. Am. Chem. Soc. **81**, 678 (1959).

[9] A. E. Petrarca, J. Org. Chem. **24**, 1171 (1959).

[10] I. Heilbron, Dictionary of Organic Compounds, Revised Ed., Vol. III, p. 305. Oxford University Press, New York (1953).

of the reaction mixtures were determined from mass spectral data.

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