Tetrahedron Letters No. 38, pp 3263 - 3266, 1975. Pergamon Press. Printed in Great Britain.

STEREOSPECIFIC REACTIONS OF OXIMES AND OXIME DERIVATIVES

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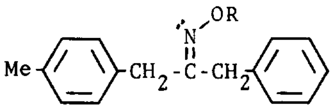
(Received in USA 4 April 1975; received in UK for publication 11 August 1975)

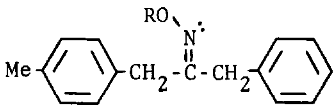
The lithium aluminum hydride (LAH) reduction of oximes is known to produce primary amines,[1] rearranged secondary amines[2,3] or aziridines[4] depending upon the reduction conditions and the substrate structure. In contrast to the Neber rearrangement,[5] the formation of aziridines *via* this method has been reported to exhibit considerable syn stereospecificity.[4] We became interested in the magnitude of this stereospecificity in oximes where little or no difference existed in the nature of the α-oximino protons, i.e., degree of substitution, molecular geometry, acidity, etc.

For this reason we undertook an examination of oximes **1a** and **2a**,



1a $R = H$

b $R = \phi\text{-}\underset{\underset{O}{\|}}{C}\text{-}$

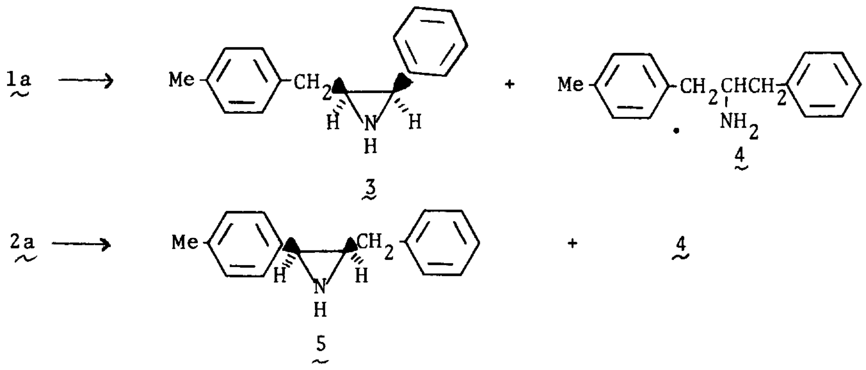


2a $R = H$

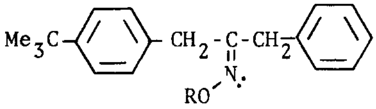
b $R = \phi\text{-}\underset{\underset{O}{\|}}{C}\text{-}$

which were prepared as a mixture from the appropriate precursor ketone. Pure samples of **1a** and **2a** were obtained by an involved fractional recrystallization procedure.[6] However, the mixture of the corresponding benzoates **1b** and **2b** was separated much more easily by fractional recrystallization,[7] and the reconversion process to the original oximes was investigated. With aqueous sodium hydroxide solution, or with sodium hydride in toluene the reconversion process was not stereospecific. However treatment of either **1b** or **2b** with sodium naphthalene[8] in tetrahydrofuran at room temperature resulted in smooth stereospecific regeneration of the corresponding oxime. The stereochemistries of the oximes were determined by stereospecific Beckmann rearrangement and confirmed by lanthanide shift reagent nmr studies as well as by nmr comparison with dibenzyl ketoxime.[9]

The LAH reduction of pure **1a** or pure **2a** in tetrahydrofuran at 66° was found to proceed with surprisingly high syn stereospecificity as a single different aziridine was obtained in high yield from each oxime upon simple recrystallization of the crude reduction product mixture. The structure assignments of the aziridines were based on the values of the geminal hydrogen coupling constants of the corresponding phenyl carbamoyl derivatives[10] and comparison nmr studies with the *cis*-aziridine formed from dibenzyl ketoxime.[11] Examination of the crude reduction mixture for each oxime (**1a** and **2a**) indicated the presence of primary amine **4** (5-15%) and small amounts of the other aziridine (< 5%). Control experiments support the contention that the minor aziridine in each case results from thermal isomerization of the starting oxime. When the reduction was carried out at room temperature the yield of the minor aziridine decreased, but the reaction mixture was contaminated with larger percentages of primary amine **4**. Thus a straight-forward sequence for the regioselective conversion of a substituted dibenzyl ketone into either of two possible aziridines has been demonstrated. The isolated yields of **3** and **5** were >80%.

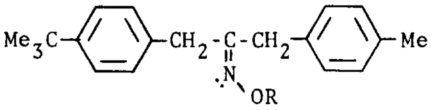


The benzoate fractional recrystallization procedure has also been used successfully in the preparation of pure samples of oximes 6a and 7a from the normal stereoisomeric mixtures obtained by oximation of the appropriate



6a R = H

6b $R = \phi-\underset{\overset{\|}{O}}{C}-$

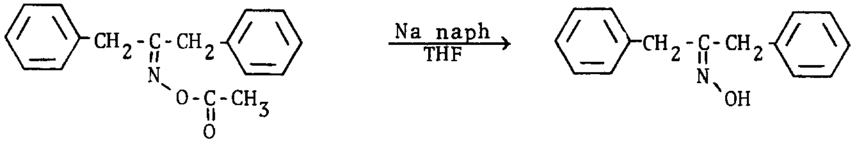


7a R = H

7b $R = \phi-\underset{\overset{\|}{O}}{C}-$

dibenzyl ketone. While benzoates 6b and 7b are easily obtained pure by fractional recrystallization, the regenerated and stereoisomerically pure oximes (6a and 7a) have resisted all efforts at crystallization. Thus the method has real utility for the separation of oxime stereoisomers that are non-crystalline or difficult to crystallize.

While no mechanistic study of the oxime benzoate cleavage process has been attempted, the ready cleavage of oxime acetate 8 under identical conditions



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would seem to indicate that the process is general for oxime carbonyl derivatives.

Acknowledgement. Appreciation is expressed for partial support of this work by The Research Corporation and the donors of the Petroleum Research Fund, administered by the American Chemical Society.

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6. Repeated recrystallization (> 20 times) of the oxime mixture from ethanol gave pure **1a**, mp 110.5-111°. Repeated recrystallization of the combined mother liquors from petroleum ether afforded pure **2a**, mp 99.5-100°.

7. The benzoates were purified in a similar but considerably easier fashion: **1b**, mp 76-76.5°, from ethanol; **2b**, mp 63-64°, from petroleum ether.

8. J. F. Garst and F. E. Barton, II, *J. Amer. Chem. Soc.*, **96**, 523 (1974). The isolated yield of oximes by this procedure was 80-90%; the normal work up involved addition of water, extraction with ether and chromatography on silica gel.

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