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STEREOCHEMISTRY OF AZIRIDINE FORMATION BY LITHIUM ALUMINUM HYDRIDE REDUCTION OF OXIMES

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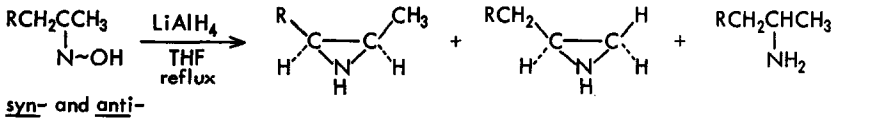
RECENTLY we reported a new method for the synthesis of aziridines by the lithium aluminum hydride (LAH) reduction of some ketoximes (1).

During the course of further studies, it was found that the reaction products were influenced by the stereochemistry of the oximes used. This is the subject of this paper.



syn- and anti-
I a: R=C_6H_5-
b: R=α-$C_{10}H_7$-

II a: R=C_6H_5-
b: R=α-$C_{10}H_7$-

III a: R=C_6H_5-
b: R=α-$C_{10}H_7$-

IV a: R=C_6H_5-
b: R=α-$C_{10}H_7$-

As reported previously (1), the LAH reduction of oily 1-phenyl propan-2-one oxime (Ia) in refluxing tetrahydrofuran (THF) gave cis-2-phenyl-3-methylaziridine (IIa) together with the normal reduction product, the primary amine IVa.

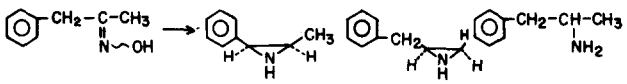
The more detailed investigation of the reduction products showed that there was another aziridine IIIa (2) reversely cyclized towards the terminal methyl group. As pure crystalline anti-form of Ia, m.p. 62-63°, could be obtained,*1 the LAH reduction of the pure anti-isomer and the oily mixture of syn- and anti-forms with a variety of content ratio was reinvestigated under the same condition and the respective reduction products were analized by the technique of gas-liquid chromatography (GLC).

As shown in TABLE I, the increase of syn-isomer caused the enhancement of cyclization to the benzylic position, resulting in the increased formation of the aziridine IIa. On the other hand, when the content of

*1 Glover and Raaen recently reported the isolation of pure crystalline anti-form of Ia (J. Org. Chem., 31, 1987 (1966)).

TABLE I

Gas chromatographic analyses of the LAH reduction products of 1-phenylpropan-2-one oxime



Ia syn, anti — **IIa** — **IIIa** — **IVa**

Isomer ratio of the oxime	Product		
	IIa	IIIa	IVa
anti only	4.7 %	18%	65 %
anti : syn = 5~7 : 1	13	13	56
anti : syn = 2~3 : 1	23	8.8	56

In each case, 300mg of the oxime was reduced by refluxing with 166mg (2.2 molar equiv.) of LAH in 10cc of THF for 2hrs., and the product mixture was analized by GLC.

anti-isomer increased, the reverse cyclization towards the terminal methyl group increased, forming the aziridine IIIa.

It was noteworthy that eventhough the pure anti-isomer was used, there was still formed a small amount of IIa, probably because of the isomerization of some of anti-form to syn-form during the reaction.*2

We also succeeded in the isolation of the pure anti-isomer of 1-α-naphthylpropan-2-one oxime (Ib) as crystalline (m.p. 96-97°). The determination of the configurations and the quantitative analyses of two isomers were performed based on the NMR data (FIG. 1).

In analogy to the case of 1-phenylpropan-2-one oxime (Ia), the LAH reduction of 1-α-naphthylpropan-2-one oxime (Ib) was carried out and the products were analized by GLC. In this case, the more clear result was obtained than that of Ia (TABLE II). Consequently it could be considered that the structures of aziridines formed were effected by the stereochemistry of the oximes used. This result was entirely different from that of the Neber rearrangement, in which the products were independent on the stereochemistry of the oximes (3).

*2 We actually found that when pure anti-oxime was refluxed in THF for 2 hours without LAH, about one tenth of anti-oxime isomerized to syn-isomer.

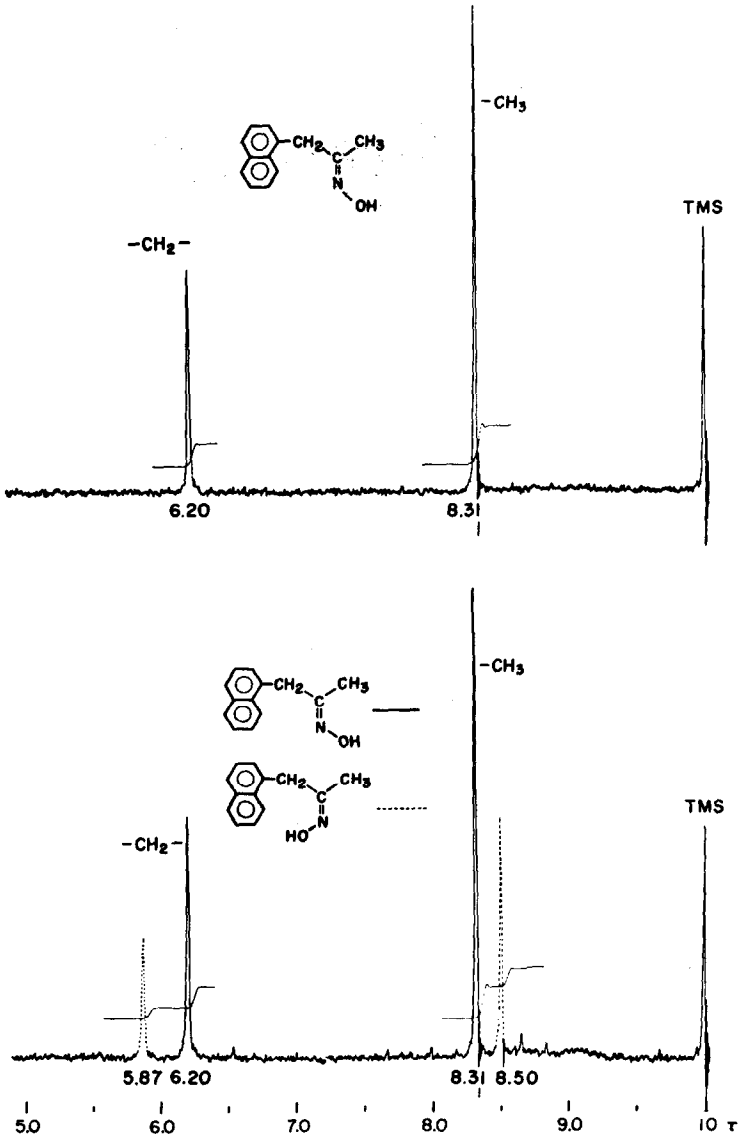
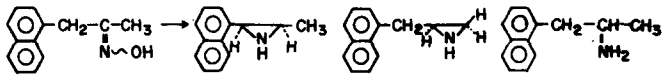


FIG. 1. NMR Spectra of 1-α-Naphthylpropan-2-one Oxime (IIb) in Benzene (60 Mc)

TABLE II

GLC analyses of the LAH reduction products of 1-α-naphthyl-propan-2-one oxime



IIb syn, anti IIIb IVb

Isomer ratio of the oxime	Product		
	IIb	IIIb	IVb
anti only	15.2%	28.9%	53.5%
anti : syn = 3.6~3.8 : 1	26.1	23.3	41.1
anti : syn = 1.3~1.4 : 1	39.0	15.0	33.3

Reduction procedure : oxime, 150mg ; LAH, 75mg (2.6 molar equiv.); THF, 5cc ; refluxed for 3 hrs.

Neither of two mechanisms (1) for this reaction, which we previously proposed based on those of the Neber and related rearrangements, can reasonably explain that the reaction products are dependent upon the configurations of the oximes. Although cyclic intermediates such as in the cases of cyclopropane formation reactions (4), or the mechanism of concerted γ-elimination leading to the retention of the configuration could be speculated, further studies are being in progress to obtain the conclusive evidences.

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