Tetrahedron Letters No.26, pp. 2197-2200, 1965. Pergamon Press Ltd.
Printed in Great Britain.

ANOMALOUS LITHIUM ALUMINIUM HYDRIDE REDUCTION OF STRECKER NITRILES DERIVED FROM INDOLE-3-ALDEHYDE

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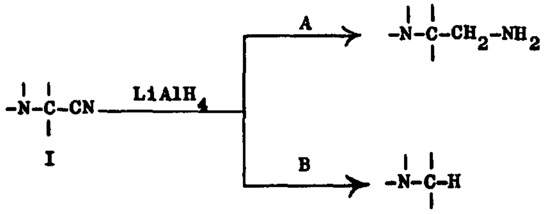
(Received 23 April 1965)

The course of $LiAlH_4$ reduction of α-aminonitriles (I) is dependent to a large extent on the substituents, besides the basic function, on the Carbon α to the nitrile group (2). Thus, when the α-carbon carrying the amino group is mono substituted or not substituted at all the reduction proceeds predominantly via path A (see below) and when it is disubstituted, the reaction mainly follows path B. In certain cases (2), however, the reduction may simultaneously go through both pathways.



The α-aminonitriles (II) prepared from benzaldehyde, substituted benzaldehydes and other aromatic aldehydes as thiophene-2-aldehyde and furfural by the Strecker reaction (3) furnished, on reduction with $LiAlH_4$, the corresponding 2-amino-2-arylethylamines (III) in high yields.

II $\xrightarrow{LiAlH_4}$ III

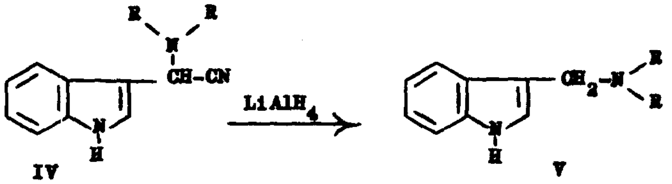
a. Ar = Phenyl R = $-(CH_2)_2-O-(CH_2)_2-$

b. Ar = 3,4-Methylenedioxyphenyl R = $-(CH_2)_5-$

c. Ar = 2-Furyl R = $-(CH_2)_5-$

d. Ar = 2-Thienyl R = $-(CH_2)_5-$

On the contrary, the $LiAlH_4$ reduction of the Strecker nitriles (IV) derived from indole-3-aldehyde resulted in the displacement of the nitrile group with the formation, in excellent yields, of the 3-amino-methylindoles (V) which were identified by comparison (m.p. and I.R. Spectra) with authentic samples prepared from indole through the Mannich reaction (4).



IV $\xrightarrow{LiAlH_4}$ V

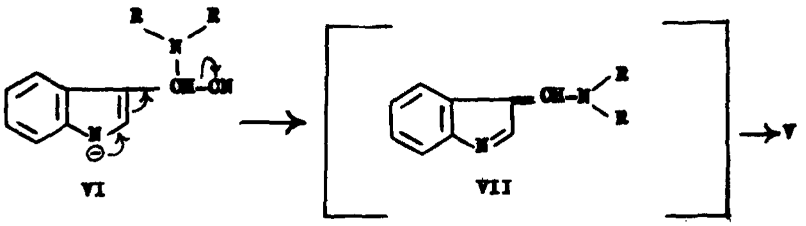
a. R = $-(CH_2)_4-$

b. R = $-(CH_2)_5-$

c. R = $-(CH_2)_6-$

d. R = $-(CH_2)_2-O-(CH_2)_2-$

This anomalous reaction of the compounds of the type IV can be rationalised on the basis of the mechanism outlined below.

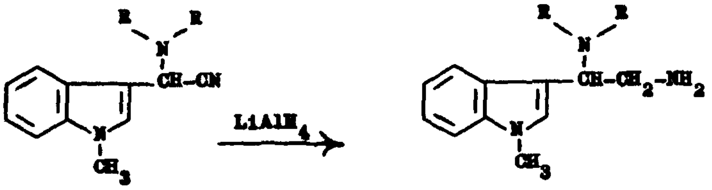


VI

VII

The anion (VI), initially formed by the attack of the reducing species at the 1-position of IV, displaces the nitrile group as the cyanide ion in a series of electronic shifts and the enamine type of intermediate (VII) thus generated undergoes reduction to V.

If this postulation is correct, then by blocking the 1-position of the α-aminonitriles (IV) it should be possible to effect the normal reduction of the nitrile function with LiAlH$_4$. Accordingly, Strecker nitriles (VIII) were prepared from 1-methylindole-3-aldehyde and subjected to reduction with LiAlH$_4$ whereby compounds of the type IX were obtained in good yields and were characterised as their ureas and thioureas (5).



VIII

IX

a. R = $-(CH_2)_5-$

b. R = $-(CH_2)_6-$

c. R = $-(CH_2)_2-O-(CH_2)_2-$

Details of this work will shortly be published elsewhere.

Acknowledgement: We would like to thank Professor T. R. Govindachari for his interest in this work, Dr. K. Nagarajan for helpful discussions and Dr. S. Selvavinayakam and his staff for elemental analyses and infrared spectra.

References

1. To whom inquiries pertaining to this communication should be directed.
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5. Satisfactory elemental analyses were obtained for all new compounds described in this communication.