# A Novel Ring Expansion Reaction in the Reduction of Benzylic Methoxyamines with Lithium Aluminium Hydride

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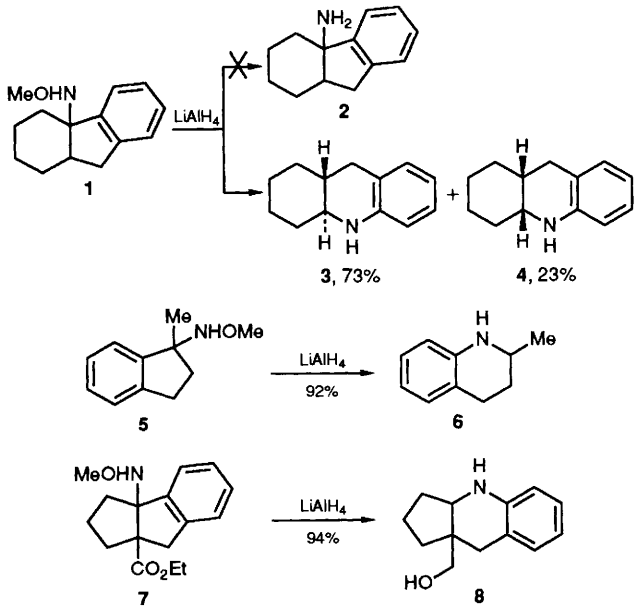
Reduction of the N–O bonds of benzylic hydroxylamines with lithium aluminium hydride gives a novel ring expansion reaction that can be explained by a radical mechanism.

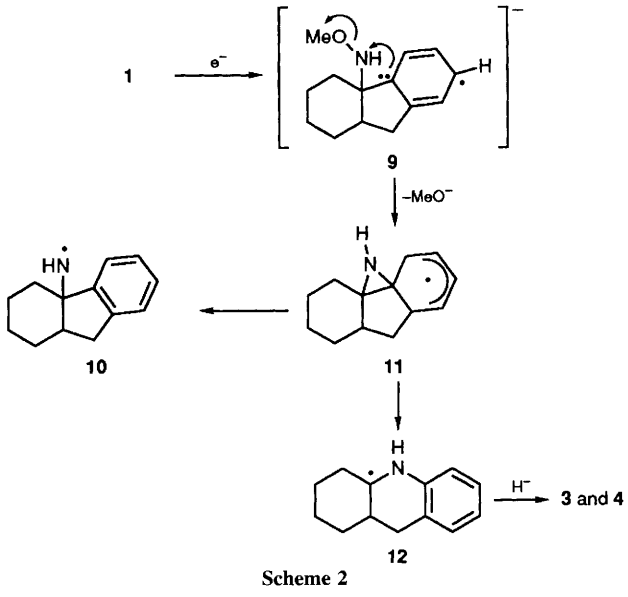
We recently reported the intramolecular cyclisation of vinyl and aryl radicals on to oxime ether acceptors to give five-, six- and seven-membered rings.[1] Part of these studies was the reduction of the N–O bond of the methoxyamine products to produce the corresponding amines. Several methods are available for the reduction of the N–O bond,[2] but initial attempts at reduction using aluminium amalgam,[3] samarium diiodide[4] and zinc–acetic acid were unsuccessful. The attempted reduction of the N–O bond of **1** with lithium aluminium hydride ($LiAlH_4$) resulted in an unexpected rearrangement which is the subject of this communication.

4a-Methoxyaminocyclohex[*a*]indan **1** in anhydrous diethyl ether was reacted with $LiAlH_4$ at reflux temperature for 2 h under nitrogen. Chromatography of the product mixture gave two pure solids (19:6 ratio) in 96% overall yield.† Mass spectrometry indicated that the two products were isomers ($M$ = 147), but neither of the products were the expected 4a-aminocyclohex[*a*]indan **2**. The IR spectra showed, in each case, only a single N–H stretching vibration instead of the expected two strong bands for the primary amine **2**. The $^1H$ NMR spectra showed all the aromatic protons appearing at higher field than those of the starting material, strongly suggesting that a rearrangement had occurred bringing the nitrogen into conjugation with the aromatic ring. The spectroscopic evidence indicated that the products were *trans* and *cis* 1,2,3,4,4a,9,9a,10-octahydroacridine **3** and **4** with the *trans* isomer as the major product. The melting point for the *trans* compound **3** was 80–82 °C which was in agreement with the literature value.[5] In the same way 1-methoxyamino-1-methylindan **5** gave 2-methyl-1,2,3,4-tetrahydroquinoline **6**[5]† and ethyl 3a-methoxyaminocyclopent[*a*]indan **7** was converted into 1,1a,1b,3-tetrahydro-1b-hydroxymethylcyclopenta[*b*]quinoline **8** (Scheme 1).†

† Compounds **3**, **4**, **6** and **8** were fully characterised by $^1H$ and $^{13}C$ NMR spectroscopy and high-resolution mass spectrometry.




Scheme 1




Scheme 2

$LiAlH_4$ usually behaves as a hydride donor when used as a reducing group for carbonyl groups. However, in some cases, such as the reduction of carbon–halogen bonds of aryl and vinyl halides, a mechanistic study has shown that these are not simple $S_N2$ substitution reactions.[6] Reduction of vinyl halides can result in a geometrical isomerism that might suggest the involvement of a radical intermediate.[7] It is suggested that in these cases the reaction involves a single electron transfer mechanism.

A similar electron-transfer process could explain the reaction of 4a-methoxyaminocyclohex[*a*]indan **1** with $LiAlH_4$ (Scheme 2). A radical anion **9** could be formed by a one electron-transfer, subsequent decomposition leading to the stabilised radical **11**, ring opening of the strained three-membered ring would either produce the aminyl radical **10** or result in ring expansion to the six-membered ring tertiary radical **12** where the aromaticity of the benzenoid ring has also been re-established. Reaction with hydride would then give 1,2,3,4,4a,9,9a,10-octahydroacridine as a mixture of the *cis* and *trans* isomers **3** and **4** as the tertiary radical **12** can be attached by the hydride from either face. This mechanism offers a rational explanation of the observed reaction, but it can only be regarded as speculative in the absence of definitive evidence. This ring expansion of benzylic methoxyamines is related to the Beckmann type rearrangement of oximes with $LiAlH_4$.[8] A somewhat related reaction has been reported by Curran.[9]

The combination of this new rearrangement reaction with the facile synthesis of hydroxylamines by intramolecular radical cyclisation reactions promises to be a useful method for the synthesis of a number of *N*-heterocyclic natural products.

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