

First Observation of a C–CN Bond Cleavage During the Reduction of a Nitrile with LiAlH₄: a S.E.T. Reaction?

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LiAlH₄ reduction of 5-cyano-5-isopropylsulphonylnorborn-2-ene **1** gave the reduced product **2** resulting from the first reported LiAlH₄-induced C–CN bond cleavage. Preliminary observations suggest that the first step involves a S.E.T. (Single Electron Transfer).

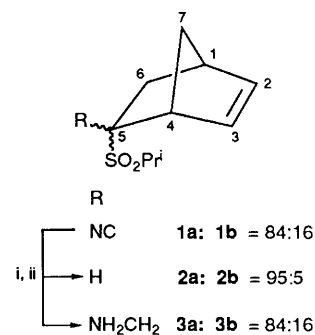
LiAlH₄ reduction of nitriles usually gives the corresponding amines, reactions which have been rationalized in terms of nucleophilic attack of a hydride anion on the cyano group.¹ Lithium aluminium hydride undergoes mainly polar reactions, nevertheless, experimental data suggest that radicals are involved during the reduction of some halides,² tosylates,³ or aromatic ketones.⁴ However, reduction of nitriles to hydrocarbons has been reported with alkali metals.⁵ Grignard reagents also display a 1-electron reducing ability toward the cyano group.⁶

We describe here the first experimental evidence for C–C bond cleavage of a nitrile induced by LiAlH₄. This nitrile is both sterically hindered and in a specific electronic environment.

During the course of studies related to the elaboration of efficient radical-clocks⁷ in the norbornenyl series we observed C–CN bond cleavage upon reduction of 5-cyano-5-isopropylsulphonylnorborn-2-ene **1** with LiAlH₄ in THF as solvent.† Starting from **1**, a mixture of the amine **3** and of the reduced product **2** was obtained in a 1:1 ratio (Scheme 1); **a** and **b** refer respectively to *endo* and *exo* isomers (position of the sulphonyl group). The overall yield of reduction was 88% together with 12% of unidentified products.

The ratios **2**:**3** and **a**:**b** were evaluated respectively by ¹H NMR and GLC analysis of the crude product. Structural evidence is based on elementary analysis, mass spectroscopy, ¹H and ¹³C NMR (NMR data are analysed in a separated publication).⁸

The steric hindrance at the C-5 bearing the cyano group and the observed stereochemistry disallow a conventional S_N2 pathway. The incorporated hydrogen atom originates from the lithium aluminium hydride as evidenced by experiments using LiAlD₄ which showed a quantitative deuteration on C-5 in compound **2**. Such a pattern of reactivity is usually reported when LiAlH₄ reacts as a 1e-reducing agent,^{2c} but does not completely exclude the possibility of hydride addition on CN followed by HCN expulsion.

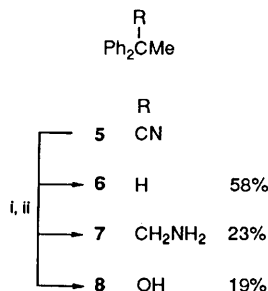


Scheme 1

In contrast with this dual reactivity of **1** towards LiAlH₄, the sulphide counterpart **4** (SO₂R replaced by SR in **1**) undergoes only the normal reduction (no C–CN bond cleavage) when treated under identical conditions with LiAlH₄. The LUMO of **1** (MNDO) lies at –2.1 eV and is mainly localized on the SO₂ (and adjacent carbons) part of the structure whereas the LUMO of **4** lies at 0.71 eV and is mainly localized on the double bond. We therefore reasoned that a low lying LUMO could make easier electron transfer⁹ and studied the reaction of 2,2-diphenylpropionitrile **5** with LiAlH₄.‡ This type of substrate

† *Typical Experimental Procedure.*—The nitrile (1 equiv.) was dissolved in dry THF and added to an heterogeneous slurry of LiAlH₄ (1.1 equiv.) in dry THF in the temperature range 0–5 °C. The mixture was stirred under nitrogen for 22 h at room temperature. Work-up involved slow hydrolysis and filtration. The filtrate was washed with saturated brine and dried (MgSO₄). Evaporation gave the crude product as an oil. Chromatography on silica gel with benzene–ethyl acetate as the eluent afforded pure the reduced products **2a** and **2b**. Further elution with ethyl acetate–methanol (90:10 and 80:20) as the eluent leads to a mixture of the isomers **3a** and **3b** of the amino compound.

‡ The thioether **4** and 2,2-diphenylpropionitrile **5** reductions were slower and the reaction time is slightly longer.



Scheme 2 Reagents: i, LiAlH₄, THF; ii, H₂O

with a geminate phenyl substituent is reported to behave as a good electron acceptor.¹¹ The results shown in Scheme 2 show that the reduction of **5** performed in an overall yield of 94% also follows a dual pattern of reactivity. The identification of products in this reaction result from ¹H NMR, mass spectroscopy and elemental analysis. The relative quantities of products were measured by ¹H NMR analysis of the crude product.

These observations, added to the literature information which show that C–CN bond cleavage is mainly observed when excellent 1e-donors such as Na are the reducing agents,⁵ suggest that the production of **2** and **6** involves an electron transfer from the metal hydride to the nitrile. We are at present further exploring the merits of this mechanistic hypothesis in comparison with expulsion of HCN or radical chain mechanisms¹² by using more elaborate chemical and spectroscopic tools.

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