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Occurence of a Radical Intermediate During the Reductive Decyanation of an α-sulfonitrile with $LiAlH_4$

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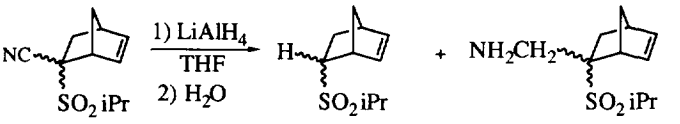
Abstract: $LiAlH_4$ reduction of 2-(isopropylsulfonyl)-bicyclo[2.2.1]hept-5-ene-2-carbonitrile **1** gave the reduced product **2** resulting from the first reported $LiAlH_4$ induced α-sulfonitrile decyanation. Experiments using $LiAlD_4$ suggest the involvement of a radical intermediate. Using a radical-probe, the spiranic compound **6** characteristic of a radical intermediate has been detected. Electrochemical measurements do fit with a SET from $LiAlH_4$ to the nitrile. Copyright © 1996 Elsevier Science Ltd

The reductive decyanation of nitriles has been achieved under several conditions. This transformation occurs principally with solvated electrons formed from alkali metals solutions.[1] The suggested mechanism involves an electron transfer with initial cyanide loss leading to the corresponding radical.[1a,b] Tertiary nitriles yield sometimes decyanation products in reactions with organometallic compounds (RLi, RMgX).[2] Decyanation of geminal dinitriles promoted by Bu_3SnH[3] or SmI_2[4] has also been efficiently achieved. Usually α-aminonitriles are transformed into amino derivatives via an iminium intermediate by reductive decyanation using $NaBH_4$ or $LiAlH_4$.[5] The proposed mechanism is a S_N1 pathway with assistance of the amino group and formation of an iminium ion intermediate.[5c, d] We have previously reported the first cleavage of an α-sulfonitrile induced by $LiAlH_4$. When 2-(isopropylsulfonyl)-bicyclo[2.2.1]hept-5-ene-2-carbonitrile **1** was reduced with $LiAlH_4$ in THF as solvent (Scheme 1), a mixture of the amine **3** and of the reduced product **2** was obtained in a 1 : 1 ratio (62% isolated yield, mass balance: 88%).[6] N and X refer respectively to endo and exo isomers (position of the sulfonyl group).[7] The S_N1 pathway cannot take place in this case. Moreover, steric hindrance and the poor leaving group ability of CN^- cannot be reconciliated with a S_N2 pathway. We now present evidence to support the occurrence of radical intermediates in this new reductive decyanation using isotopic labelling, radical-probe and electrochemistry.

The reduction of nitrile **1** (1 eq., 0.27M) with $LiAlD_4$ (1.1 eq.) leads to a 96% deuterium incorporation (mass spectroscopic analysis). Reduction in a more diluted medium where the concentration of nitrile **1** is 0.10 M gives only 90% of deuterium incorporation.[8] This observation hints at a competition between the hydride and the solvent as hydrogen atom donors. If a radical intermediate abstracts a hydrogen atom from solvent or a deuterium

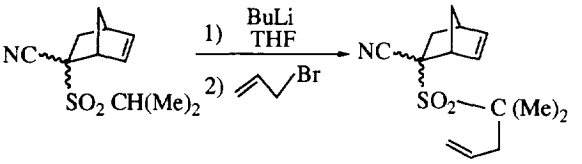
Scheme 1



1 (N/X = 84/16) **2** (N/X = 95/5) **3** (N/X = 84/16)

atom from $LiAlD_4$, then less concentrated solution results in a lower deuterium content due to a lower $LiAlD_4$ solvent ratio. This result suggests that α-sulfonitrile **1** is reduced by a radical pathway.[9] Free radical intramolecular additions are one of the most popular tools used to demonstrate the occurence of radical intermediates on a reaction pathway. The 5-hexenyl rearrangement has previously been found to be a good radical probe since the cyclisation is fast ($k_{cy} = 10^5\ s^{-1}$, 25 °C),[10] irreversible and selective.[11] So we prepared norbornene **4** (N/X = 80/20 from ^1H NMR spectroscopy) in 80% yield by alkylation of the carbanion formed from **1** in a basic medium (Scheme 2) with allylbromide.

Scheme 2

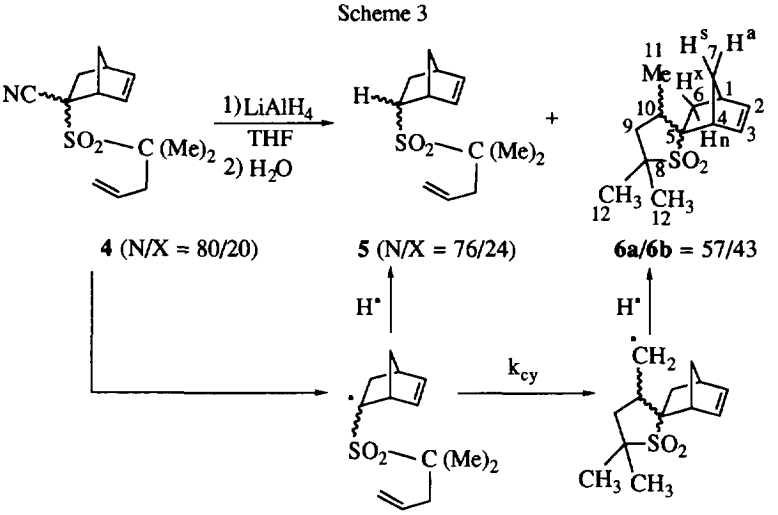


1 (N/X = 80/20) **4** (N/X = 80/20)

The reduction of **4** (N/X = 80/20) with $LiAlH_4$ afforded four decyanated products (17% yield) isolated after two chromatographies on silica gel: the linear products **5N-X** and a mixture of the cyclised products **6a** and **6b** (**5/6** = 80/20). The ratios **5/6**, **5N/5X** and **6a/6b** were determined from ^1H NMR and GC analysis. The structure of **6a-6b** was established from mass spectroscopy and high resolution NMR (^1H, ^{13}C, ^1H-^1H COSY) analysis.[12] The preferential 5-membered ring formation results from an exo mode closure[13] of the non stabilized α-sulfonyl radical.[14] The formation of the cyclic sulfones **6a** and **6b** is highly suggestive of a radical intermediate. We did not try to isolate the amines homologous to **3** in the reaction displayed in Scheme 3.

$LiAlH_4$ mainly reacts by polar reactions, nevertheless experimental data suggest that electron tranfer can be involved especially with halides,[15] alcohols,[16] polynuclear hydrocarbons,[17] hindered sulfonates[18] or benzylic methoxyamines.[19] We have observed that the sulfide counterpart of **1** (SO_2 replaced by SR), undergoes only the normal reduction. 2,2-Diphenylpropionitrile, a better electron acceptor, undergoes the C-CN bond cleavage.[6] These observations lead us to consider the feasibility of an ET from the hydride to the cyano group. House discussed as possible electron transfer between carbanionic nucleophiles and unsaturated carbonyl compounds in terms of the difference in standard electrode potentials.[20] He concluded that with $E^o_{A/A^{\bullet-}} - E^o_{D^{\bullet+}/D}$ (D = donor, A = acceptor) more positive than - 0.4 V (corresponding to $\Delta G° < 9.2$ kcal mol^{-1}) the electron transfer would be feasible. Eberson applied Marcus theory to estimate postulated electron transfer processes involving carbanionic nucleophiles. He estimated the standard potential of $AlH_4°/AlH_4^-$ redox couple as -(0.1-0.3 V) vs NHE in THF.[21] Taking the value $E^o_{H°/H^-}$ as -0.3 V the electron transfer from $LiAlH_4$ to nitrile **1** would be relatively fast if $E^o_{1/1^{\bullet-}}$ was larger than -0.7 V. Taking into account this value, we measured the $E_{1/2}$ value of the nitrile **1** (cyclic voltammetry). No reduction wave was found till -2.2 V vs SCE (conc $=10^{-3}$ M, 0.1M TBAHFP

Scheme 3



in CH_3CN; $E_{1/2\ (1/1^{\circ-})}$ < -1.96 V vs NHE). Contrary to aromatic sulfones, aliphatic sulfones are electrochemically reduced only with an activating group such an olefin.[22] Moreover nitriles are poor electron acceptors and our data reflect the difficulty of reduction of the nitrile functional group.[23] As previously described, the C-CN bond cleavage is mainly observed when excellent $1e^-$-donors such as Na ($E^{\circ}_{Na^+/Na}$ = -2.72 V vs NHE in HMPT)[20] are the reducing agents.

A variety of methods have been utilized in order to elucidate the mechanism of this new decyanation reaction. If radical intermediates have been detected, electrochemical data discard the possibility of an electron transfer from $LiAlH_4$ to the nitrile group. This reduction could therefore proceed via a radical chain mechanism for which the initiation step remains obscure. The propagation step probably involves an S_H2 reaction of the radical intermediate to yield the decyanated product and the radical anion of AlH_3.[24]

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12. The position of the sulfonyl and methyl (-CH_3 13) groups has not been established definitively.^{1}H NMR (400 MHz, $CDCl_3$, coupling constants in Hz). **6a**: 6.40 (dd, J = 6, 3, H_2); 6.32 (dd, J = 6, 3, H_3); 2.93 (m, H_4); 2.91 (m, H_1); 2.36 (d quintuplet, J = 9, 7, H_{10})*; 1.96 (dd, J = 14, 7, H_9)*; 1.74 (dd, J = 13, 3, H_{6x}); 1.72 (dd, J = 13, 9, H_9)*; 1.69 (ddd, J = 13, 3, 1, H_{6n}); 1.57 (dm, J = 9, H_{7s}); 1.40 (ddt, J = 9, 2, 2, H_{7a}); 1.33 (s, H_{12})*; 1.25 (s, H_{12})*; 1.20 (d, J = 7, H_{11})*. **6b**: 6.32 (dd, J = 6, 3, H_2); 6.29 (dd, J = 6, 3, H_3); 3.14 (m, H_4); 2.93 (m, H_1); 2.47 (dqd, J = 13, 7, 5, H_{10})*; 2.27 (dd, J = 12, 3, H_{6n}); 1.86 (dd, J = 13, 5, H_9)*; 1.64 (dd, J = 12, 4, H_{6x}); 1.56 (m, H_{7a}); 1.49 (dm, J = 9, H_{7s}); 1.43 (t, J = 13, H_9)*; 1.34 (s, H_{12})*; 1.23 (s, H_{12})*; 1.09 (d, J = 7, H_{11})*. * possible reversal of assignments between **6a** and **6b**. Consideration of cyclisation transition states on Darling molecular models suggests that the major isomer **6a** corresponds to SO_2 group on the same side as the methylene norbornenyl bridge and the methyl group exo with respect to the norbornenyl group. The other one **6b** would correspond to an SO_2 group on the side opposite to the methylene bridge and the methyl group still exo with respect to the norbornenyl group.
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