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ANOMALOUS LITHIUM ALUMINUM HYDRIDE REDUCTION OF CARBON-CARBON DOUBLE BONDS IN 7-AZABICYCLO(2.2.1)HEPTENYL SYSTEMS

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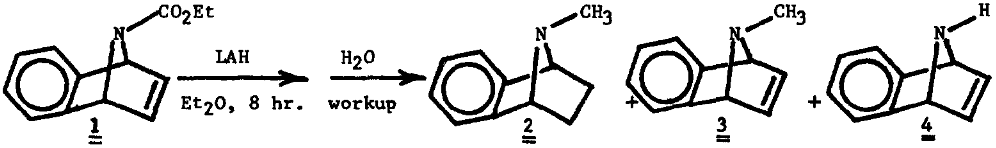
Recent interest in the mechanism of lithium aluminum hydride (LAH) reductions of formally isolated carbon-carbon double bonds[1-6] prompts us to report our observations for the corresponding reductions in azabicyclic systems.

N-Carbethoxy-7-aza-2,3-benzobicyclo(2.2.1)heptadiene (1, mp 59.5-60.0°) was prepared via Diels-Alder addition of benzyne[7] to N-carbethoxypyrrole. Reduction of 1 with LAH or Vitride in diethyl ether afforded three products, (2-4). The reaction products were separated by glpc utilizing a ¼ in. by 10 ft. FFAP (20%, on Chromasorb W) column, (column temp. = 155°, He flow rate = 120 ml./min.). Product identification was accomplished via nmr and mass spectral analysis.



product ratios· 33 61 6

Deuterium labeling studies were performed in an effort to delineate the mechanism of the reduction. Treatment of 1 with LAH followed by workup with NaOD-D$_2$O afforded 2-d_1 along with 3 and 4. The position of the deuterium atom in 2 was established as *exo*-5- (or 6-) by comparison of the nmr spectrum of 2-d_1 (figure 1.b) with that of 2-*exo*,*exo*-5,6-d_2 (prepared via D$_2$/Pd-C reduction of 3,[8] figure 1.c). The corresponding reduction of 1 with lithium aluminum deuteride (LAD) followed by workup with NaOH-H$_2$O afforded 2-d_4, whose structure was assigned by analysis of its nmr spectrum, (figure 1.d).

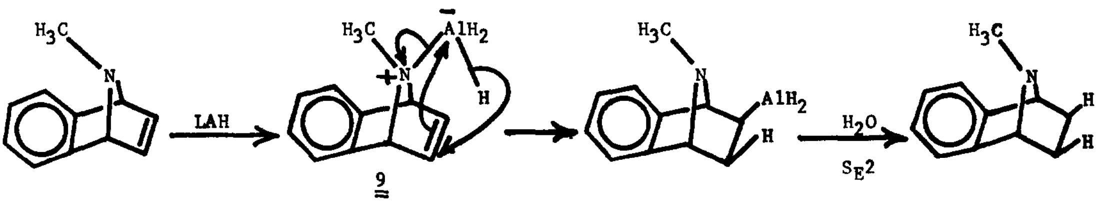
In a separate experiment, it was determined that 3 could be reduced smoothly to 2 by LAH-Et$_2$O under the same conditions whereby 3 is generated via reduction of 1. This result suggests that 3 may be an intermediate in the overall LAH reduction of 1 to 2.

Interestingly, no 7-aza-2,3-benzonorbornene (5) was observed among the products of the reduction of 1. In a separate experiment, reduction of 4[9] to 5 occurred under conditions whereby 1 is reduced to 2-4. However, the reduction of 4 was observed to be much more sluggish than is the corresponding reduction of 1. This observation probably accounts for the absence of 5 among the products of the LAH reduction of 1.

We have extended our studies of LAH reductions of azabicyclics to include two related systems· N-carbethoxy-7-azanorbornene[10] (6) and N-methyl-5-azabicyclo(2.2.2)oct-2-ene[11] (7). Interestingly, LAH reduction of 6 afforded N-methyl-7-azanorbornane[10] (8) as the only reaction product. However, no reduction product was obtained when 7 was similarly treated with LAH-Et_2O. To explain these observations, we look to subtle differences between the geometries of the anticipated organoaluminum intermediates derived via the reactions of LAH with systems 6 and 7, (*vide infra*). An additional contributing factor might lie in the anticipated differences in strain energies in proceeding from 6 to 8 as compared with the case of proceeding from 7 to the corresponding saturated system.[12]

The closest analogy to our observed LAH-promoted C=C reductions lies in an earlier report by Franzus and Snyder[2]. These investigators studied the corresponding LAH reductions of norbornenes and norbornadienes bearing oxygen-containing substituents (-OH, -OAc, and -O*t*-Bu) in the *syn*-7-position.[2] An intramolecular mechanism for these reductions was proposed. An analogous mechanism for the corresponding reductions in our 7-azabicyclo(2.2.1)heptenyl systems is shown in Scheme I. Note that a

SCHEME I



four-center transition state is implied for the intramolecular reduction of the 5,6-double bond (9, Scheme I). To the best of our knowledge, the reduction of 3 to 2 and of 6 to 8 represent the first reported examples of LAH reductions of formally isolated double bonds in bicyclic amine systems.

The markedly different behaviour of 6 and of 7 toward LAH-Et_2O suggests that relief of strain may be an important factor (in addition to the previously-recognized[2] importance of geometric configuration) in facilitating anomalous double-bond reductions by LAH. Additional experiments designed to clarify this point and to further delineate the detailed mechanism of the reduction process are underway. We hope to report the results of these studies shortly.

Figure 1. (Shown on next page). Partial 60 MHz nmr spectra ($CDCl_3$ solvent, aromatic proton region not shown) of (a) N-methyl-7-aza-2,3-benzonorbornene, (2); (b) N-methyl-7-aza-2,3-benzo-exo-5-deuterionorbornene, (2-d_1); (c) N-methyl-7-aza-2,3-benzo-exo,exo-5,6-dideuterionorbornene, (2-exo,exo-5,6-d_2); (d) N-trideuteriomethyl-7-aza-2,3-benzo-exo-5-deuterionorbornene, (2-d_4).

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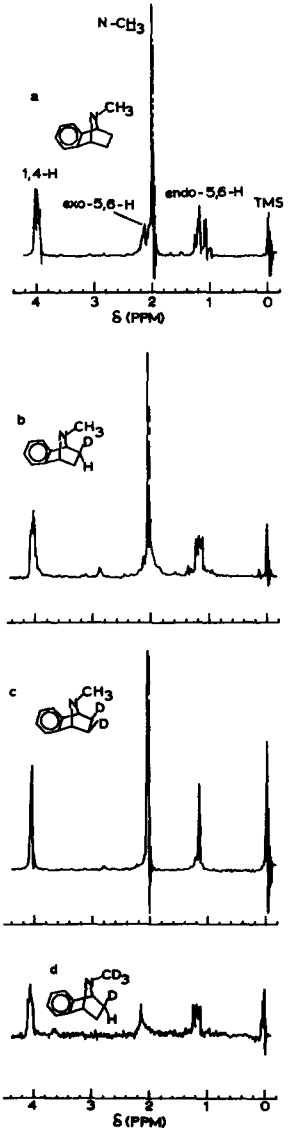
N-CH3
a
N
CH3
1,4-H
exo-5,6-H
endo-5,6-H
TMS
4
3
2
1
0
δ (PPM)
b
N
CH3
D
H
c
N
CH3
D
D
d
N
CD3
D
H
4
3
2
1
0
δ (PPM)