# Effects of Metal Alkoxides on the Lithium Aluminium Hydride Reduction of Substituted Prop-2-ynyl Alcohols

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THE reduction of substituted prop-2-ynyl alcohols and the related aldehydes, acids, *etc.*, to *trans*-allylic alcohols[1] has been of considerable synthetic use.[2] Under more forcing conditions,[3] $LiAlH_4$ will reduce simple alkyl and aryl acetylenes. It has been assumed[4] that the alcohol reduction reaction is analogous to the reduction of cinnamyl alcohols: an internal addition of hydride to the 2-carbon, from an oxygen-bonded aluminium hydride, coincides with the development of a *trans*-vinyl carbanion at the 3-carbon. Presumably the developing carbanion is stabilised to some extent by another aluminium atom. Intermolecular hydride donation to the 2-carbon, with stabilization of the developing 3-carbanion by oxygen-bonded aluminium remains a possibility.[5] Quenching of the products from these reactions (both with iodine[6] and deuterium oxide[7]), shows that the predominant mode of addition of the aluminium hydride to the triple bond is of the first type, although small quantities of products from the reverse mode leading to the 2-carbanion, were detected. Corey[6] has shown that the addition of sodium methoxide, or aluminium chloride, to the reaction mixture resulted in the exclusive formation of the 3- or 2-carbanion, respectively. During attempts to utilize Corey's procedure for the synthesis of some *cis*-1-hydroxyalkylvinyl halides, we found some unusual effects of added alkoxide on reaction rate (Table).

TABLE

| Substrate alcohol and reducing system | % Reduction[b] | | | | |
|---|---|---|---|---|---|
| | 1 Hr. | 2 Hr. | 4 Hr. | 6 Hr. | 22 Hr. |
| (I) Prop-2-yn-1-ol | | | | | |
| $LiAlH_4$ | 82 | 96 | 98 | 99 | 100 |
| $LiAlH_4$ + NaOMe | 66 | 76 | 83 | 86 | 92 |
| $LiAlH_4$ + $KOBu^t$ | 2 | 3 | 4 | 6 | 9 |
| (II) Oct-1-yn-3-ol | | | | | |
| $LiAlH_4$ | 44 | 69 | 88 | 93 | 96 |
| $LiAlH_4$ + NaOMe | 80 | 86 | 90 | 93 | 97 |
| $LiAlH_4$ + $KOBu^t$ | 1 | 2 | 3 | 4 | 10 |
| (III) Oct-2-yn-1-ol | | | | | |
| $LiAlH_4$ | Complete | | | | |
| $LiAlH_4$ + NaOMe | Complete | | | | |
| $LiAlH_4$ + $KOBu^t$ | Complete | | | | |
| (IV) Hex-2-yn-4-ol | | | | | |
| $LiAlH_4$ | Complete | | | | |
| $LiAlH_4$ + NaOMe | Complete | | | | |
| $LiAlH_4$ + $KOBu^t$ | Anomalous[c] | | | | |
| (V) Ethynylcyclohexanol | | | | | |
| $LiAlH_4$ | 6 | 9 | 16 | 24 | 67 |
| $LiAlH_4$ + NaOMe | 76 | 86 | 92 | 95 | 98 |
| $LiAlH_4$ + $KOBu^t$ | 1 | 1 | 1·5 | 2 | 4 |
| (VI) 1-(Prop-1-ynyl)cyclohexanol | | | | | |
| $LiAlH_4$ | 32 | 67 | 97 | 100 | — |
| $LiAlH_4$ + NaOMe | Complete | | | | |
| LiAlHR + $KOBu^t$ | Anomalous[c] | | | | |

[a] All reactions were carried out in refluxing tetrahydrofuran
0·067M in alcohol
0·1M in lithium aluminium hydride
0·2M in added alkoxide

[b] The results indicated are the mean of four analyses on each of two or more experiments. The reactions were sampled at the times noted, the sample was hydrolysed, extracted, and analyzed by vapour phase chromatography using a 6 ft. × $\frac{1}{4}$ in. 10% Carbowax 20 M on Chromosorb W column in a Hewlett Packard Model 5750 chromatograph. All results are corrected for relative responses.

[c] The reduction of these two carbinols in the presence of potassium t-butoxide resulted in a rapid disappearance of starting material but little allyl alcohol formation.

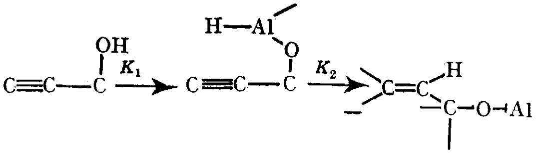
Little elimination of acetylide occurred, except with old samples of potassium t-butoxide (presumably contaminated with hydroxide and/or carbonate), and also with sodium hydride as the added base, when elimination was the major process.

To summarise:

1. The rate of reduction of ethynyl carbinols is markedly reduced by the addition of potassium t-butoxide.
2. The addition of sodium methoxide causes a significant enhancement in reduction rate especially in cases where there is some degree of steric hindrance at carbinol oxygen.

The first case presumably results from formation of the acetylide anion with subsequent electrostatic repulsion of attacking hydride. This observation could permit the selective inhibition of reduction of a terminal ethynyl carbinol during the $LiAlH_4$ reduction of some other function in the molecule; thus reduction of 7-methylnona-2,8-diyne-1,7-diol with $LiAlH_4$ afforded 7-methylnona-*cis*-2,8-diene-1,7-diol (90%); whereas, in the presence of potassium t-butoxide, 7-methylnona-*cis*-2-ene-8-yne-1,7-diol (60%) was obtained.

The second case appears more complex. The ease of reduction of substituted prop-2-ynyl alcohols, together with the anti-Markovnikov addition of aluminium hydride (*cf.* ref. 3) suggests a mechanism involving oxygen–aluminium bonding:



The first step in this process, oxygen–aluminium bond formation ($k_1$), should be subject to steric influences; however, the subsequent intramolecular hydride donation ($k_2$) should not. The rate of reduction in the absence of added alkoxides is markedly dependent upon steric factors (Table). This implies that step 1 is rate-determining.

The rates of reduction of the three ethynyl alcohols (I), (II), and (V) differ markedly in the absence of methoxide: however, they are nearly identical with added methoxide. We feel that this last rate is essentially that of the hydride delivery step, which in an ethynyl alcohol would show some inhibition by acetylide ion formation. This would be the overall result of acceleration of step 1 by methoxide.

In the non-terminal acetylenes the absence of any possibility of rate inhibition by acetylide ion formation leads to the generally greater rates in the presence of added methoxide. Our results would seem to rationalize Corey's observations[6] regarding the effect of sodium methoxide on the orientation of addition due to an acceleration of the hydroxy-oriented addition relative to the thermal Markovnikov addition.

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