213. The Reductive Conversion of Some Cyclic and Acyclic *vic*-Epoxides to Alcohols by Means of Lithium Aluminium Hydride/Aluminium Trichloride

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Unsubstituted medium-ring 1,2-epoxycycloalkanes and certain *vic*-epoxyalkanes are reduced to the corresponding alcohols very slowly when $LiAlH_4$ alone is used as reducing agent. However, the combination of $LiAlH_4$ and $AlCl_3$, in a 2:1 molar ratio (with respect to 1 mol-equiv. of epoxide) used in refluxing Et_2O, greatly enhances these reductions, rendering them of interest for practical purposes.

In [1] [2], we showed that the ease of reductive opening of the oxirane rings by $LiAlH_4$ for 1,2-epoxycycloalkanes depends on the size of the carbocyclic ring and the configuration *(cis-trans)* of the oxirane system. Medium-ring 1,2-epoxycycloalkanes were particularly resistant to $LiAlH_4$ reduction, and, moreover, *trans*-epoxides suffered C–O bond cleavage more difficultly than the corresponding *cis*-isomers *(Table)*.

To shorten the reaction times and thus make this conversion of epoxides to alcohols of practical utility, we have now studied the reduction of unsubstituted 1,2-epoxycycloalkanes using $LiAlH_4$ in combination with $AlCl_3$[1]). However, since such mixtures can produce, in dependence of the relative proportions of the components, various 'mixed hydrides', whereby products other than alcohols may be also formed [3] [4], consequently the influence of the $LiAlH_4/AlCl_3$ molar ratio on the product distribution was first investigated. It was found that an epoxide/$LiAlH_4/AlCl_3$ molar ratio of 1:2:1 (in Et_2O at 35°) gave the best results, the only (or essential) products of oxirane-ring opening being the desired alcohols (98–100%), which could be isolated in over 90% yield[2]). Moreover, this reactant ratio caused reduction of 1,2-epoxycycloalkanes to occur much faster than with $LiAlH_4$ alone (up to 50 times and more), and even medium-ring 1,2-epoxycycloalkanes were completely cleaved after short reaction times (15–210 min) (see *Table*). Here also the *trans*-1,2-epoxycycloalkanes were reduced more slowly than the *cis*-

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[1]) The $LiAlH_4/AlCl_3$ combinations have been used for the reduction of various functional groups [3].

[2]) With different reactant ratios, in addition to the desired alcohols, various other products were also obtained. (To be published.)

Table. *Ease of Reduction of Some 1,2-Epoxycycloalkanes and* vic-*Epoxyalkanes to Alcohols with $LiAlH_4$ alone (mol-ratio epoxide/$LiAlH_4$ 1:2)* [1] [2] *and with $LiAlH_4$/$AlCl_3$ (mol-ratio epoxide/$LiAlH_4$/$AlCl_3$ 1:2:1), in Refluxing Et_2O* a)

Epoxide	Reaction times for oxirane ring opening b)	
	with $LiAlH_4$ [h]	with $LiAlH_4$ + $AlCl_3$ c) [min]
1,2-Epoxycycloalkanes		
1,2-Epoxycyclopentane *(cis)*	~ 0.5	5
1,2-Epoxycyclohexane *(cis)*	~ 0.1	< 1
1,2-Epoxycycloheptane *(cis)*	3	5
cis-1,2-Epoxycyclooctane	48 (24%)	15
cis-1,2-Epoxycyclodecane	48 (76%)	120
trans-1,2-Epoxycyclodecane	48 (96.5%)	210
cis-1,2-Epoxycyclododecane	12 (2.5%)	30
trans-1,2-Epoxycyclododecane	48 (28%)	45
cis-1,2-Epoxycyclopentadecane	12 (1%)	30
trans-1,2-Epoxycyclopentadecane	24 (4%)	35
vic-*Epoxyalkanes*		
1,2-Epoxyoctane	< 0.1 d)	< 1 d)
1,2-Epoxydecane	< 0.1 d)	< 1 d)
cis-2,3-Epoxyhexane	1 e)	5 e)
trans-2,3-Epoxyhexane	2 (2.5%) f)	15 f)
cis-3,4-Epoxy-2,5-dimethylhexane	24 (3%)	60
trans-3,4-Epoxy-2,5-dimethylhexane	30 (3%)	75

a) The reductions were performed with 1–2 mmol of epoxide, in 15–30 ml of Et_2O (see *Exper. Part*).

b) The reaction times refer to complete reductions, except in the cases when percent values are cited in parentheses, these values indicating the amount of unreacted epoxide (after the given time).

c) According to GLC, the yields of alcohols were 98–100%. In some cases, Cl-containing and olefinic products were detected in trace amounts.

d) Products: 2-alkanol/1-alkanol (99–100):(1–0) ($LiAlH_4$); (97–98):(3–2) ($LiAlH_4$ + $AlCl_3$).

e) Products: 3-hexanol/2-hexanol 53.5:46.5 ($LiAlH_4$); 58:42 ($LiAlH_4$ + $AlCl_3$).

f) Products: 3-hexanol/2-hexanol 52:48 ($LiAlH_4$); 55:45 ($LiAlH_4$/$AlCl_3$).

isomers, but the difference in reaction times was much less than was the case for reductions with $LiAlH_4$ alone *(Table)*.

A similar rate enhancement was observed in the $LiAlH_4$/$AlCl_3$ reductions of some *vic*-epoxyalkanes (see *Table*). The *cis*-epoxides were again reduced faster than the corresponding *trans*-compounds.

It could be inferred that the reduction of epoxides with the $LiAlH_4$/$AlCl_3$ 2:1 combination is an electrophilically assisted reaction, in which the reducing agent attacks preferentially the more substituted oxirane C-atom [3] [4]. However, the ratios of 2-alkanol/1-alkanol products obtained from 1,2-epoxyalkanes *(Table, Footnote d)* are very similar to those observed in the corresponding $LiAlH_4$ reductions *(Table)*, and this would indicate that the mechanism in both cases is of the S_N2 type. In the presence of $AlCl_3$, electrophilic catalysis by AlH_3, $AlClH_2$, and other species³) enhances the reductive process but without noticeably changing the direction of the oxirane ring cleavage, *i.e.*

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³) With the $LiAlH_4$/$AlCl_3$ molar ratio of 2:1 (for 1 mol-equiv. of epoxide) used in the present study, different reactive species can be envisaged [3] [4] to exist in the reaction mixture, such as $LiAlH_4$, AlH_3, $AlClH_2$, $AlCl_2H$, *etc.*

without decreasing the predominance of attack of the reducing agent at the less substituted (less sterically hindered) epoxy C-atom.

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Experimental Part

General. See [2].

The reductions with $LiAlH_4/AlCl_3$ (using a molar ratio epoxide/$LiAlH_4/AlCl_3$ 1:2:1) were performed with 1–2 mmol of epoxide and the required amounts of $LiAlH_4$ and $AlCl_3$ in 15–30 ml of dry Et_2O at 35°, in a similar way as described previously for the $LiAlH_4$ reductions [2], *i.e.* n mmol of epoxide in $n \cdot 5$ ml of Et_2O was added dropwise, at r.t., to a stirred suspension containing $2n$ mmol of $LiAlH_4$ and n mmol of $AlCl_3$ in $n \cdot 10$ ml of Et_2O (n being 1 or 2), whereupon the resulting mixture was heated to boiling. Aliquots were taken at definite time intervals and analyzed by GLC for unreacted epoxide, alcohol produced, and other (if any) reaction products. The results obtained are given in the *Table.*

In larger scale runs, performed with 0.03–0.06 mol of epoxide (and the necessary quantities of $LiAlH_4$ and $AlCl_3$), the alcohol product was isolated, after the usual workup [2], by distillation or column chromatography. The yield was, in general, over 90%.

It should be noted that the $LiAlH_4/AlCl_3$ combination in Et_2O was prepared by simple addition of the components to dry Et_2O (cooled in ice-cold water), and the resulting suspension used *as such, i.e.* without previous filtration.

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