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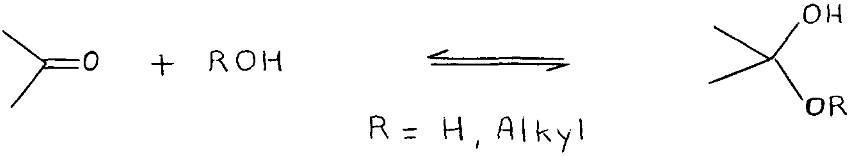
LANTHANOIDS IN ORGANIC SYNTHESES 7[1].
SELECTIVE REDUCTIONS OF CARBONYL GROUPS IN AQUEOUS ETHANOL SOLUTION.

by A.L. Gemal and J.L. Luche*
LEDSS - Université Scientifique et Médicale
BP 53 X - 38041 Grenoble Cédex - France

Summary: Trivalent lanthanoid ions were shown to permit the selective reductions of conjugated aldehydes in the presence of non-conjugated ones. $CrCl_3$ is also effective in selective ketone reduction in the presence of aldehydes.

Selective modification of similarly reactive functional groups is a challenging problem in organic synthesis. We have recently shown that the selective reduction of the less reactive of two carbonyl groups (ketone or aldehyde) can be achieved by $NaBH_4$ in the presence of lanthanoid derivatives by two complementary procedures. The first one is performed in methanol and involves an in situ ketalization as the intermediate step[2], the second one is effected in aqueous ethanol with the formation of an unstable protective species, either a hemiketal or a hydrate[3]. In this paper new results are reported for the selective reductions of conjugated aldehydes in the presence of non-conjugated ones. In some cases the ketone-aldehyde discrimination is also shown to be obtained by the means of $CrCl_3$ instead of lanthanoid chlorides.

Addition of ROH (R = H or alkyl) to a carbonyl group is a general acid catalyzed reaction[4] and the hydration equilibrium has been shown to be rapidly established.



Theoretical models of these reactions have been investigated recently[5]. Although kinetic measurements have shown that alcohols (MeOH > EtOH) add more readily than water[6], to our knowledge no unambiguous study has been performed in mixed solvents. In the above mentioned reaction, the unstable carbonyl derivative involved in the reductive process in ethanol-water solution is most probably the hydrate[7], which can be stabilized by the lanthanoid ion through a chelating effect. If this were so, it can be anticipated that the selectivity of our reduction process can roughly be correlated to the selectivity of the hydration. As it is known that conjugated aldehydes are usually less hydrated than non conjugated ones[4,8], application of the selective hydration process should allow the selective reduction of conjugated aldehydes in the presence of non conjugated ones. The results presented in table 1 confirm this expectation. This method thus appears to complement the ketalization method in which

TABLE 1

Aldehyde selective reductions in aqueous ethanol in the presence of $ErCl_3$[a].

Starting mixture	% reduction[b]
Benzaldehyde	93 (88)[c]
1,2,5,6 tetrahydrobenzaldehyde	11 (29)[c]
Benzaldehyde	95
Hexanal	12
Benzaldehyde	85
Hexahydrobenzaldehyde	0
Citral	80
Hexanal	13
Citral	100
Citronellal	13
2-Thiophene carboxaldehyde	85
Hexahydrobenzaldehyde	0

[a] for the standard procedure see ref. 3. 1.5 Molar equiv. $NaBH_4$ (i.e. a 6 fold excess of hydride) is used. Various experiments have shown that selectivity is optimal under these conditions.

[b] from VPC measurements. Complement to 100% is the starting material.

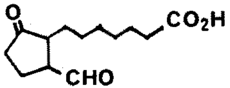
[c] the reagent was $CeCl_3 \cdot 6H_2O$.

a similar selectivity cannot be obtained due to the ease of ketal formation of most aldehydes.

The superiority of lanthanoid derivatives in these selective transformation was indicated in our previous paper[3]. Among the derivatives of other elements tested, the best results were obtained with chromium trichloride. Table 2 gives some exemples of these competitive reductions. Thus it appears that in some cases chromium derivatives can effectively replace those of lanthanoids.

TABLE 2

Selective reductions in the presence of Er^{3+} and Cr^{3+}

Starting mixture	% reduction[a] with $ErCl_3$	with $CrCl_3$
2-Octanone	98	52
1,2,5,6, tetrahydrobenzaldehyde	14	19
Acetophenone	98	93
1,2,5,6 tetrahydrobenzaldehyde	14	18
Cyclohexanone	100	95
Hexanal	2	13
Benzaldehyde	93	92
1,2,5,6, tetrahydrobenzaldehyde	11	14
Cyclohexanone	100	90
Hexahydrobenzaldehyde	15	22
	85 (75)[b]	– (52)[b]

[a] Calculated yield from VPC measurements. Complement to 100% is the recovered starting material.

[b] Isolated yield (column chromatography on silica gel) of the aldehyde alcohol.

TABLE 3

Selective reductions in the presence of Lanthanoid derivatives.

Compounds	Acetalization Method	Hydration Method
Non conjugated aldehydes	-	-
Conjugated aldehydes	-	+
Non hindered ketones	-	+
Hindered or conjugated ketones	+	+

+ (-) implies that the compound can(not) be reduced under the specified conditions.

Table 3 summarizes the selective reductions and reminds that the ketalization method is preferred to reduce hindered or conjugated ketones in the presence of unhindered ones.

Thus the combination of the hydrate method and the selective ketalization process offers possibilities to reduce at will carbonyl groups of various kinds. A limitation that has not yet been resolved is the selective reductions of non-hindered ketones in the presence of conjugated aldehydes. Both series of compounds are easily ketalized and are only slightly hydrated. Notwithstanding this restriction, the catalytic properties of lanthanoid derivatives offer a very useful set of methods in the field of selective reductions.

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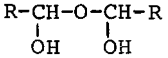
References

1. Preceeding paper in this series: Gemal, A.L. and Luche, J.L., *J. Am. Chem. Soc.*, in press.
2. Gemal, A.L. and Luche, J.L., *J. Org. Chem.* (1979), **44**, 4187.
3. Luche, J.L. and Gemal, A.L., *J. Am. Chem. Soc.* (1979), **101**, 5848.
4. Ogata, Y. and Kawasaki, A., in "The Chemistry of the carbonyl group", vol. 2, Interscience publishers, New York 1970; Hurd, C.D., *J. Chem. Educ.* (1966), **43**, 527; Jencks, W.P., *Chem. Reviews* (1972), **72**, 705; Greenzaid, P., Luz, Z., Samuel, D., *J. Am. Chem. Soc.* (1967), **89**, 749; Hooper, D.L., *J. Chem. Soc. B* (1967), 169. In the case of aldehydes, hemihydrates **1** have been isolated in some cases. See: Klass, D.L., Jensen, W.N., Blair, J.S. and Martinek, T.W., *J. Org. Chem.* (1963), **28**, 3029; Hardy, P.M., Nicholls, A.C., and Rydon, H.N., *J. Chem. Soc. Perkin Trans 2* (1972), 2270.



$$\underset{OH}{R-CH}-O-\underset{OH}{CH}-R$$

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5. Williams, I.H., Maggiora, G.M., and Schowen, R.L., *J. Am. Chem. Soc.* (1980), **102**, 7831.
6. Le Hénaff, P., *Bull. Soc. Chim. Fr.* (1968), 4687.
7. That the hemiketal is not present is indicated by a solvent variation. Mixtures of water with methanol, ethanol or isopropanol give similar selectivity in the competitive reduction of hexanal and cyclohexanone. The stabilizing effect of the Ln^{3+} ion on the hydrate can be deduced from experiments run in THF water mixtures: in this solvent the selectivity is greatly decreased. This result can be accounted for by the strong coordinating ability of THF, which binds to the Ln^{3+} ion in the place of the gem diol.
8. The position of the hydration equilibrium depends on the structure of the carbonyl compound. Whether this position is modified or not by the Ln^{3+} ions will be discussed in the final paper.

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