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Selective Catalytic Hydrogenation in the Presence of Lanthanide *tris*-β-Diketonates as "Protecting" Reagents

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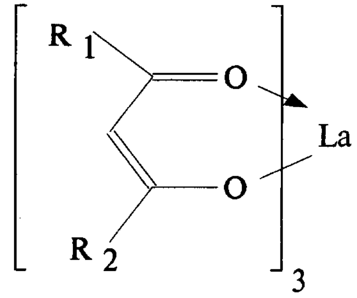
Abstract. The selectivity of >C=C< double bonds catalytic hydrogenation increases considerably in the presence of some lanthanide *tris-β*-diketonates for those unsaturated aldehydes and ketones possessing highly susceptible to reduction carbonyl group. It is a result of the selective co-ordination between the lanthanide complex added and the carbonyl group of a substrate. In most cases the complete protection of carbonyl groups is observed if the complex is added in equimolar amount to the substrate. A number of lanthanum *tris–β*-diketonates have been tested; the complexes with fluorinated ligands were demonstrated to ensure the highest selectivity of the hydrogenation. The correlation between the constants of equilibrium in reaction mixture and "protecting" activity of the complexes is discussed. A few examples demonstrate the practical utilization of the lanthanum *tris-β*-diketonates to the selective hydrogenation of unsaturated aldehydes and ketones.

In a previous paper[1], we reported that the presence of some lanthanide *tris–β*–diketonates in a reaction mixture often causes the reactivity of substrate functional groups to decrease. This phenomenon can be attributed to the co-ordination of the lanthanide *tris–β*–diketonates with the functional groups. The co-ordination is known to be selective: lanthanide chelates are "hard" Lewis acids and complex preferentially to "hard" Lewis base groups[2]. These facts apparently suggest that the lanthanide *tris–β*–diketonates can be utilized to selective functional group protection in varied transformations of multifunctional molecules. Thus, catalytic hydrogenation of unsaturated aldehydes in the presence of $La(fod)_3$ (fod - 2,2-dimethyl-6,6,7,7,8,8,8-heptafluoro-3,5-octanedionato-) leads only to the corresponding saturated aldehydes[1]. Being co-ordinated to the lanthanum chelate, even highly susceptible to reduction carbonyl groups remain intact under these reaction conditions. Contrary to the usual techniques, this method of carbonyl group protection does not require the isolation of the compounds with the protected groups; one need only to carry out the desired reaction of a substrate in the presence of equimolar amount of the lanthanide complex. The lability of the adducts formed by lanthanide *tris–β*–diketonates allows to separate the complexes readily from the reaction end products.

In principle, the approach which has been described for hydrogenation[1] can be utilized to other reactions. We have reported[3] the usage of lanthanide *tris–β*–diketonates in selective alkylation of difunctional compounds. Moreover, there is the unique opportunity to use wide experience in chemistry of lanthanide complexes, especially in the field of lanthanide shift reagents[2], for the further elaborating of this approach and for the prediction of its effectiveness in real applications. It is of interest to investigate the effect of ligand nature on the "protecting" ability of lanthanide complexes.

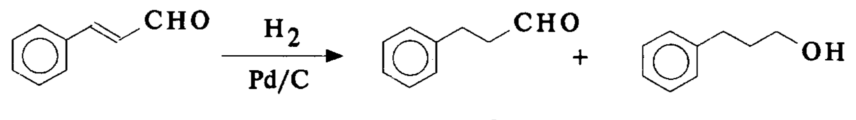
This article discusses the results of comparison studies of different lanthanum *tris*–*β*–diketonates **1-6** as the auxiliary reagents for carbonyl group protection. We also give here some examples of selective carbon-carbon double bond hydrogenation for those unsaturated substrates which possess very susceptible to reduction carbonyl groups.

1, La(fod)$_3$, R_1 = t-Bu, R_2 = C_3F_7;
2, La(pta)$_3$, R_1= t-Bu, R_2 = CF_3;
3, 3La(tfa)$_3$·THF, R_1= CF_3, R_2 = CH_3;
4, La(bta)$_3$,, R_1 = Ph, R_2 = CF_3;
5, La(bac)$_3$, R_1 = Ph, R_2 = CH_3;
6, La(acac)$_3$, R_1 = R_2 = CH_3;



We have taken the hydrogenation of *trans*-3-phenylpropenal (cinnamaldehyde, 7) at atmospheric pressure of hydrogen over palladium on activated carbon (Pd/C) as a model reaction for the investigation. ^{1}H-NMR spectroscopy is very convenient to follow the reaction which has been carried out in deuterated solvents in an NMR sample tube. The complexes **1-6** are diamagnetic, so their presence in the reaction mixture does not make the interpretation of the NMR spectral data difficult as it would be in the case of their paramagnetic analogues because of large NMR signal shifts and broadenings.

Palladium on carbon is known to be one of the most effective heterogeneous catalysts for selective hydrogenation of carbon-carbon double bond in unsaturated aldehydes and ketones. However, such selective reactions are quite problematic when carbonyl groups of the substrate are conjugated to >C=C< double bonds or to an aromatic ring. Cinnamaldehyde is one of the examples: its hydrogenation on Pd/C leads to a mixture of 3-phenylpropanal and 3-phenylpropanol:



7 **8** **9**

The effectiveness of carbonyl group protection in the presence of a complex can be assessed by a comparison of 3-phenylpropanal yields after the complete hydrogenation of 7 with and without the complex in the reaction mixture. The results of our experiments are shown in Table 1.

It can be seen that the lanthanum complexes with fluorinated ligands **1-3** exhibit the most and approximately equal "protecting" activity. Among them La(pta)$_3$ is readily available and can be recommended for practical applications. Unfortunately, addition of the most available complex --La(acac)$_3$-- as well as La(bac)$_3$ to the reaction mixture does not improve the yield of **8**.

It may be suggested that the lanthanide complex "protecting" ability depends on the constants of the equilibrium involving co-ordination of the functional group to be protected with the complex:

$$R + S \overset{K_1}{=} RS \qquad (1)$$

$$RS + S \overset{K_2}{=} RS_2 \qquad (2)$$

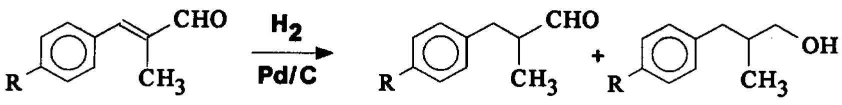
S - an organic substrate, R - the lanthanide complex.

Other equilibrium may also be important, for example:

$$R + R = R_2 \qquad (3)$$

It is difficult to obtain these equilibrium constants for lanthanum complexes with satisfying accuracy using NMR spectral data, because the NMR shifts induced by diamagnetic lanthanum ion are small. The constants values could be roughly estimated by the constants for corresponding paramagnetic europium complexes. Although the binding constants to carbonyl groups are subject to variation for different lanthanide, the values of K_1 do not vary greatly for lanthanum and europium chelates, as has been noted in literature[2]. Following the procedure described recently[2], we have found the constants K_1 and K_2 for the equilibrium between **7** and europium complexes $Eu(fod)_3$, $Eu(pta)_3$ in C_6D_6. Paramagnetic ^1H-NMR shifts values induced by these complexes were taken for the calculation which has been performed on the assumption that only the equilibrium (1) and (2) are dominant in the solution and the europium complexes co-ordinate to the carbonyl group of **7** exclusively. The K_1 and K_2 values obtained are listed in Table 2. One would expect the values of the same order for the equilibrium between **7** and corresponding lanthanum complexes **1**, **2**, and **6** which have been used for protection. Judging from the equilibrium constants values for $Eu(fod)_3$ and $Eu(pta)_3$ one can suggest that the lanthanum complexes **1** or **2** tie up the majority of aldehyde **7** molecules on RS and RS_2 adducts. The concentration of the free cinnamaldehyde molecules which supposedly react with hydrogen forming the by-product **9** is very low. However, even in the presence of equimolar amounts of **1** or **2** the carbonyl group of **7** is not completely protected. In contrast to the aldehyde **7**, non-conjugated aldehydes[1] and ketones (*vide infra*) undergo only carbon-carbon double bond hydrogenation under the same conditions. Complete protection of the carbonyl group in the presence of $La(fod)_3$ or $La(pta)_3$ is observed even for cinnamaldehyde derivative, 2-methyl-3-phenylpropanal (**10**), though the corresponding equilibrium constants K_1 and K_2 (for $Eu(fod)_3$ and $Eu(pta)_3$) in this case are less then for **7** (see Table 2). It seems plausible that in the case of **7** the equilibrium (1) and (2) are shifted to dissociation of RS and RS_2 on the catalyst surface.

We exemplify here the synthetic utilization of lanthanide *tris*-*β*-diketonates to selective carbonyl group protection by the hydrogenation of cinnamaldehyde derivatives **10**, **11** with Pd/C as catalysts. This reaction usually leads, if any, to corresponding saturated aldehydes **12**, **13** with low yields. The yields range from zero in methanol to 44% in benzene (see Table 1). The presence of $La(fod)_3$ or $La(pta)_3$ in the reaction mixture (solvent - benzene or cyclohexane) considerably improves the yields (Table 1). The final aldehydes can be isolated as bisulfate addition compounds by usual working-up procedures.



10, R=H
11, R=i-Pr

12, R=H
13, R=i-Pr

It is of interest to examine the possibility to protect from hydrogenation, if necessary, carbonyl groups of unsaturated ketones employing lanthanide chelates **1** or **2**. With this in mind we carried out first the catalytic hydrogenation of a model mixture which consists of equimolar amounts of acetophenone and cyclohexene in deuterated cyclohexane without and in the presence of La(fod)$_3$. Experimental results obtained from NMR data are shown on Fig. 1.

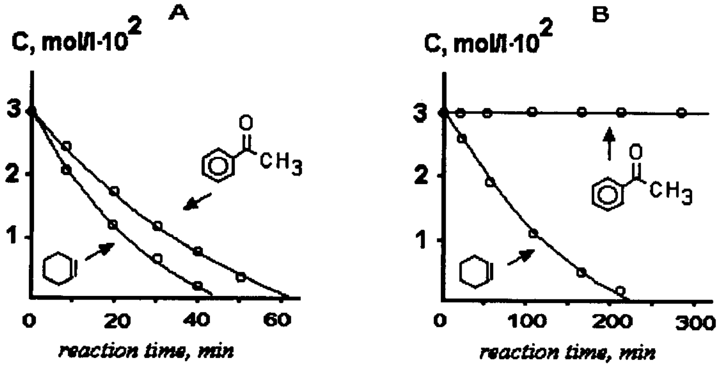
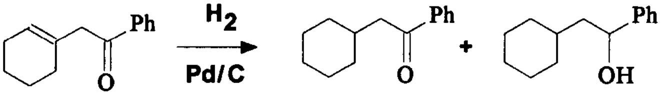


Fig.1 Acetophenone and cyclohexene concentrations during catalytic hydrogenation of their equimolar mixture in deuterated cyclohexane: A) without any complexes in the reaction mixture; B) in the presence of La(fod)$_3$, [La(fod)$_3$]=$3 \cdot 10^{-2}$ mol/l. (The catalyst amount was equal in both of the experiments).

As is evident from the graphs on Fig. 1, the hydrogenation selectivity improves dramatically when La(fod)$_3$ is added to the reaction mixture. Such selectivity enhancement was observed, as expected, when 1-phenyl-2-(cyclohexen-1-yl)-ethanone (**14**) has been taken as a substrate. The hydrogenation in this case provides very low yield (0-30%) of saturated ketone **15**, the major final product is the saturated alcohol **16**.



14 **15** **16**

Being performed with La(fod)$_3$ or La(pta)$_3$ added to the solutions, this reaction leads to 90% of **15** in benzene and 95% in cyclohexane. The lanthanum complexes can also be isolated and used repeatedly. The necessity of using large quantities of the lanthanum *tris*-β-diketonates detracts from the method described above, but the possibility to reuse the complexes makes up for this deficiency.

Table 1. The Yields (%) of Saturated Aldehydes 8,12,13 after Hydrogenation of 7,10, 11 Respectively Without and in the Presence of Equimolar amount of the Lanthanum Complexes 1-6. (Solvent - C_6D_6, unless otherwise indicated, 1 bar H_2,Pd/C 20°C).

	without complex	La(fod)$_3$	La(pta)$_3$	3La(tfa)· THF	La(bta)$_3$	La(bac)$_3$	La(acac)$_3$
Yield of 8,	59	74	77	78	63	55	45
Yield of 12	40	97	95	-	-	-	-
	0(CD_3OD)	-	-	-	-	-	-
	44(C_6D_{12})	-	-	-	-	-	-
Yield of 13	50	80	83	-	-	-	-

Table 2. The Constants K_1 and K_2 (M^{-1}) Calculated for the Equilibrium Between Eu(fod)$_3$, Eu(pta)$_3$ and Aldehydes 7, 10 in Deuterated Benzene Solutions

Complex	Compound	K_1	K_2
Eu(fod)$_3$	3-phenyl-propanal	254	42
Eu(pta)$_3$	-"-	50	2
Eu(fod)$_3$	2-methyl-3-phenylpropanal	170	10
Eu(pta)$_3$	-"-	43	11

EXPERIMENTAL

^{1}H-NMR spectra were measured with Bruker WP-100SY spectrometer (100,13 MHz for protons), TMS was used as an internal standard. Data acquisition was performed with the relaxation delay of 10 sec. before each scan to ensure the proper NMR signal intensities.The equilibrium constants K_1 and K_2 (Table 2) were calculated on PC 386 DX computer using the calculating program based on the "two-step method"[2]. First, the ^{1}H-NMR signal shifts induced by Eu(fod)$_3$ or Eu(pta)$_3$ were found for the aldehydes **7** and **8**. The "best" values of K_1 and K_2 as well as bound shifts for **RS** and **RS$_2$** complexes were found by regression analysis minimizing the discrepancies (parameter Q) between experimental and calculated induced shifts. We calculated the map of Q values in the expected area of the equilibrium constants before the iteration procedure in order to appraise properly the starting K_1 and K_2 values used for the regression. It proved useful because of multiextremal profile of the minimized function Q. The complexes **1- 5** were prepared from lanthanum nitrate and corresponding sodium enolate in aqueous ethanol, and dried *in vacuo* over P_4O_{10}.

Preparation of 3La(tfa)$_3$.THF. Anhydrous $La(NO_3)_3$ (3.25 g, 10 mmol) was dissolved in 40 mL of dry THF. Na(tfa) (5.28 g,10 mmol) in 40 mL THF was added to the solution and the resulting mixture was stirred at 40°C for 2 h. Sodium nitrate was filtered off, the solvent was removed, and the solid obtained was dried for 5 h *in vacuo*. From analytical and ^{1}H-NMR data, the yellow product approximately corresponds to the formula 3La(tfa)$_3$·THF.

Catalytic hydrogenation of 7 as well as the model mixture of cyclohexene and acetophenone was carried out in an NMR sample tube. Before the hydrogenation, the stock solution of **7** or the model mixture was prepared in an appropriate deuterated solvent, the concentration of the substrates was about 10^{-2}M. Weighted amount (10 mg) of Pd/C (palladium content 4%) was placed in an NMR sample tube together with 0.6 mL of the stock solution, and then equimolar (calculated on the aldehyde or ketone) amount of a lanthanum complex was added. This mixture was hydrogenated by bubbling hydrogen through it so as the catalyst was even suspended in the solution. ^{1}H-NMR spectra were measured from time to time to follow the process. It takes usually up to 5 h for the aldehyde or ketone to be hydrogenated completely that is evidenced by the escaping of their ^{1}H-NMR signals from the spectra.

The procedures of the preparative hydrogenation were similar for the aldehydes **12**, **13** and ketone **15**. A typical procedure is given below.

Hydrogenation of 14 to the corresponding saturated ketone 15 .

La(pta)$_3$ (1.40 g, 1.92 mmol) was dissolved in 10 mL of dry benzene. This solution and 200 mg of Pd/C (palladium content 4%) were placed in an apparatus for hydrogenation. Pure dry hydrogen was blown through the solution and then 380 mg (1.9 mmol) of **14** was added. The mixture was stirred under 1 bar of hydrogen (ambient temperature) till equimolar volume of it (46.2 mL) had been reacted. The catalyst was then filtered off and the filtrate was passed through a silica gel column (4x40 cm) with benzene as eluant that gave **15** in 90% yield and the lanthanum complex.

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