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Meerwein–Ponndorf–Verley-type reductive acetylation of carbonyl compounds to acetates by lanthanide complexes in the presence of isopropenyl acetate

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Abstract

Meerwein–Ponndorf–Verley-type reductive acetylation of carbonyl compounds to acetates was successfully carried out in the presence of isopropenyl acetate under the influence of a catalytic amount of $Ln(O^iPr)_3$ at room temperature. Various carbonyl compounds were converted into the corresponding acetates in fair to good yields. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: lanthanide; carbonyl compound; isopropenyl acetate; acetylation; Meerwein–Ponndorf–Verley reduction.

The Meerwein–Ponndorf–Verley (MPV) reduction of carbonyl compounds to alcohols by the use of a stoichiometric amount of $Al(O^iPr)_3$ in 2-propanol is a well-established method.[1] This is a mild and relatively inexpensive route for reduction of aldehydes and ketones to alcohols. Recently, the MPV reduction was reported to be efficiently promoted by lanthanide isopropoxides, $Ln(O^iPr)_3$, under mild conditions.[2] In a previous paper, we showed that the acetylation of a wide variety of alcohols with isopropenyl acetate can be achieved by samarium compounds such as $Cp^*{}_2Sm(thf)_2$ and $Sm(O^iPr)_3$ under neutral conditions.[3] Thus, tertiary alcohols which are labile under acidic and basic conditions are successfully acetylated by this method in good yields. During this study, we found that ketones are reacted in the presence of $Ln(O^iPr)_3$, in particular $Gd(O^iPr)_3$ and $Sm(O^iPr)_3$, and isopropenyl acetate at room temperature, giving acetates in fair to good yields. This reaction is referred to as MPV-type reductive acetylation of ketones to acetates, since our reaction is analogous to the MPV reduction of ketone which is prompted by $Sm(O^iPr)_3$ in the presence of an alcohol such as 2-propanol in place of isopropenyl acetate (Eq. (1)).

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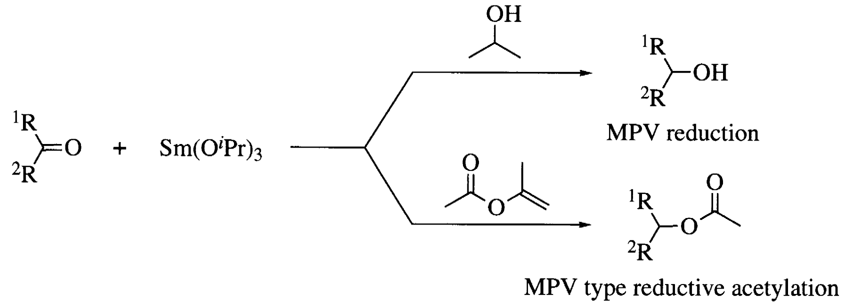
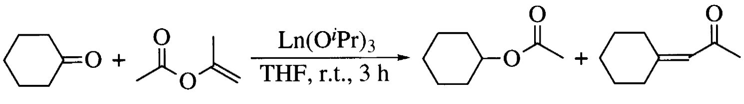


(1)

For instance, the reaction of cyclohexanone (**1a**) (1 mmol) with Sm(O^{i}Pr)$_3$ (0.67 mmol) in the presence of isopropenyl acetate (**2**) (4 mmol) in THF (6 mL) at room temperature for 3 h afforded cyclohexyl acetate (**3a**) in 83% selectivity at 88% conversion along with cyclohexylideneacetone (**4a**) (15%) which is derived from an aldol reaction of **1a** with acetone liberated from Sm(O^{i}Pr)$_3$ and/or **2**. This shows that the hydrogen transfer from the isopropoxy moiety of Sm(O^{i}Pr)$_3$ to **1a** followed by acetylation with **2** easily takes place under mild conditions.

To know the effectiveness of lanthanide alkoxides in the present reaction, several lanthanide isopropoxides^5 were allowed to react with **1a** in the presence of **2** (Table 1). Gd(O^{i}Pr)$_3$ also promoted the MPV-type reductive acetylation of **1a** to **3a** in good selectivity (Run 2). The same reaction using Yb(O^{i}Pr)$_3$ gave **3a** in a similar selectivity as that using the Sm(O^{i}Pr)$_3$, although the conversion was low (43%) (Run 3). La(O^{i}Pr)$_3$ resulted in **3a** together with a substantial quantity of an aldol condensation product **4a** (Run 4).

Table 1
MPV-type reductive acetylation of cyclohexane (**1a**) to cyclohexyl acetate (**3a**) by several metal isopropoxides in the presence of isopropenyl acetate (2)[a]



1a **2** **3a** **4a**

Run	Alkoxide	Conv. (%)	Select. (%)[b]
1	Sm(O^{i}Pr)$_3$	88	83 (15)
2	Gd(O^{i}Pr)$_3$	81	88 (7)
3	Yb(O^{i}Pr)$_3$	43	80 (16)
4	La(O^{i}Pr)$_3$	57	61 (36)
5	Al(O^{i}Pr)$_3$	no reaction	
6	Zr(O^{i}Pr)$_4$	no reaction	

[a] **1a** (1 mmol) was allowed to react in the presence of metal isopropoxide (0.6 mmol) and **2** (4 mmol) in THF (6 mL) at room temperature for 3 h under Ar atmosphere. [b] Number in parentheses represents the selectivity of cyclohexylideneacetone (**4a**) derived from aldol reaction of **1a** with acetone.

It is interesting to note that Al(O^{i}Pr)$_3$, which is employed for the MPV reduction of ketones, was completely inert for the present MPV-type reductive acetylation (Run 5). Similarly, the MPV type reductive acetylation was not induced by $\mathrm{Zr(O^iPr)_4}$ (Run 6), although $\mathrm{Zr(O^tBu)_4}$ promoted the MPV reduction.[4] These results show that the reactivity of $\mathrm{Ln(O^iPr)_3}$ is quite different from that of $\mathrm{Al(O^iPr)_3}$ or $\mathrm{Zr(O^tBu)_4}$ in these reactions.

If the present MPV-type reductive acetylation can be carried out by a catalytic amount of $\mathrm{Ln(O^iPr)_3}$, this method provides a new route to acetates from ketones. To achieve the MPV-type reductive acetylation via the catalytic process, it is important that $\mathrm{Ln(O^iPr)_3}$ is regenerated in the course of the reaction. Thus, the MPV-type reductive acetylation was examined by adding 2-propanol to the above reaction system (Table 2).

Table 2
MPV-type reductive acetylation of various carbonyl compounds catalyzed by $\mathrm{Ln(O^iPr)_3}$ in the presence of isopropenyl acetate **2** and 2-propanol[a]

Run	Carbonyl Compound	Catalyst	Conv. (%)	Acetate	Select. (%)
1	**1a**	$\mathrm{Gd(O^iPr)_3}$	95	**3a**	99
2	**1a**	$\mathrm{Sm(O^iPr)_3}$	92	**3a**	97
3	**1a**	$\mathrm{Yb(O^iPr)_3}$	54	**3a**	43 (64)[b]
4	**1a**	$\mathrm{La(O^iPr)_3}$	53	**3a**	62 (35)[c]
5	4-Methylcyclohexanone (**1b**)	$\mathrm{Gd(O^iPr)_3}$	96	**3b**	99
6	**1b**	$\mathrm{Sm(O^iPr)_3}$	83	**3b**	98
7	4-*t*-Butylcyclohexanone (**1c**)	$\mathrm{Gd(O^iPr)_3}$	94	**3c**	99
8	3-Methylcyclohexanone (**1d**)	$\mathrm{Gd(O^iPr)_3}$	94	**3d**	99
9	2-Methylcyclohexanone (**1e**)	$\mathrm{Gd(O^iPr)_3}$	58	**3e**	59 (40)[b]
10	2-Adamantanone (**1f**)	$\mathrm{Gd(O^iPr)_3}$	79	**3f**	60 (38)[b]
11[d]	1,4-Cyclohexanedione (**1g**)	$\mathrm{Gd(O^iPr)_3}$	91	**3g**	79 (19)[e]
12	Cycloheptanone (**1h**)	$\mathrm{Gd(O^iPr)_3}$	25	**3h**	96
13	Cyclopentanone (**1i**)	$\mathrm{Gd(O^iPr)_3}$	30	**3i**	27 (73)[f]
14	2-Octanone (**1j**)	$\mathrm{Gd(O^iPr)_3}$	33	**3j**	97
15	Benzaldehyde (**1k**)	$\mathrm{Gd(O^iPr)_3}$	90	**3k**	50 (47)[g]
16	**1k**	$\mathrm{Sm(O^iPr)_3}$	89	**3k**	55 (40)[g]
17	Cinnamaldehyde (**1l**)	$\mathrm{Gd(O^iPr)_3}$	70	**3l**	57 (26)[h]

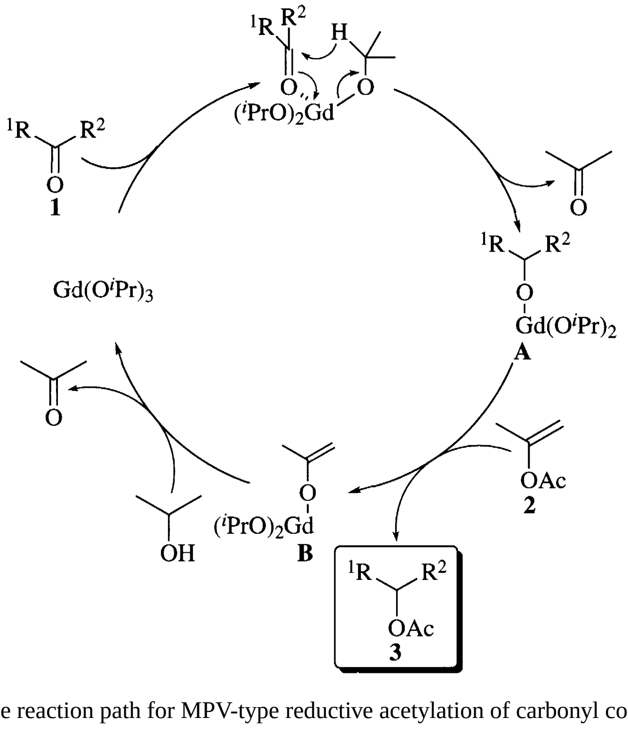
[a] Substrate (1 mmol) was allowed to react in the presence of $\mathrm{Ln(O^iPr)_3}$ (0.1 mmol), isopropenyl acetate **2** (3 mmol) and 2-propanol (4 mmol) in THF (1 mL) at room temperature for 3 h under Ar atmosphere. [b] Selectivity of alcohol. [c] Selectivity of cyclohexylideneacetone (**4a**) . [d] $\mathrm{Gd(O^iPr)_3}$ (0.2 mmol), **2** (6 mmol), 2-propanol (8 mmol) and THF (2 mL) were used. [e] Selectivity of 4-acetoxycyclohexan-1-ol. [f] Total selectivity of aldol products of **1h** itself and of **1h** with acetone, 2-cyclopentylidenecyclopentanone (**5**) (33%) and cyclopentylideneacetone (**4i**) (40%), respectively. [g] Total selectivity of aldol condensation products of benzylideneacetone (15%) and dibenzalacetone (32%). [h] Selectivity of aldol products of **1k** with acetone, 6-phenyl-3,5-hexadien-2-one.

As expected, the MPV type reductive acetylation of **1a** was promoted by a catalytic amount of $\mathrm{Ln(O^iPr)_3}$ in the presence of **2** and 2-propanol (Runs 1–4). In particular, $\mathrm{Sm(O^iPr)_3}$ and $\mathrm{Gd(O^iPr)_3}$ showed high catalytic activity to give **3a** in good yields. The formation of aldol product **4a** by $\mathrm{Sm(O^iPr)_3}$ and $\mathrm{Gd(O^iPr)_3}$ was negligibly small when 2-propanol was added to the reaction system. Unlike $\mathrm{Gd(O^iPr)_3}$

and Sm(O^{i}Pr)$_3$, the reaction by Yb(O^{i}Pr)$_3$ gave cyclohexanol rather than **3a** as a major product (Run 3). The catalytic activity of La(O^{i}Pr)$_3$ was lower than that of Gd(O^{i}Pr)$_3$ and Sm(O^{i}Pr)$_3$ to result in **3a** and a considerable quantity of **4a** (Run 4).

On the basis of these results, the MPV-type reductive acetylation of a variety of carbonyl compounds by Gd(O^{i}Pr)$_3$ and Sm(O^{i}Pr)$_3$ under these conditions was examined (Table 2, Runs 5–17). Substituted cyclohexanones, such as 4- methyl, 4-*tert*-butyl and 3-methylcyclohexanones **1b**, **1c** and **1d**, respectively, were acetylated to form the corresponding acetates in high yields (Runs 5–8). However, 2-methylcyclohexanone (**1e**) and 2-adamantanone (**1f**) were converted into the corresponding acetates **3e** and **3f** in moderate selectivities (Runs 9 and 10). 1,4-Cyclohexanedione (**1g**) was acetylated to diacetate, 1,4-diacetoxycyclohexanone (**3g**) (Run 11). The reaction of cycloheptanone (**1h**) led to the corresponding acetate **3h** in low conversion (25%), but the selectivity was high (96%) (Run 12). Treatment of cyclopentanone (**1i**) under these conditions produced cyclopentylidene-cyclopentanone (**5**) and cyclopentylideneacetone (**4i**), which are derived from homo- and cross-aldol reactions of **1i** and of **1i** with acetone, respectively, in preference to the acetate **3i** expected (Run 13). The MPV reduction of **1i** by Al(O^{i}Pr)$_3$ is reported to lead to the aldol condensation product **5** rather than cyclopentanol as a major product.[6] 2-Octanone (**1j**) was acetylated to **3j** in high selectivity (97%), although the conversion of **1j** was 33% (Run 14). Benzaldehyde (**1k**) and cinnamaldehyde (**1l**) gave acetates **3k** and **3l**, and the corresponding aldol products (Runs 15–17).

The present MPV-type reductive acetylation of carbonyl compounds by Gd(O^{i}Pr)$_3$ is outlined as Scheme 1. The reaction may be initiated by hydride transfer from the isopropoxy moiety of Gd(O^{i}Pr)$_3$ to ketone to form a gadrinium alkoxide (**A**) as an intermediate. The resulting alkoxide **A** is subjected to the acetylation by isopropenyl acetate to form acetate **3** and the resulting gadrinium enolate (**B**) readily reacts with 2-propanol to regenerate Gd(O^{i}Pr)$_3$. In the case of the Yb(O^{i}Pr)$_3$-catalyzed reaction, the **A** reacts easily with 2-propanol in preference to **2** to form alcohols as major products (Table 2, Run 3).



Scheme 1. A possible reaction path for MPV-type reductive acetylation of carbonyl compounds to acetates

Acknowledgements

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