$Zn(ClO_4)_2 \cdot 6H_2O$ as a Powerful Catalyst for a Practical Acylation of Alcohols with Acid Anhydrides

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Dedicated to Prof. Paolo Edgardo Todesco on the occasion of his 70th birthday

Keywords: Acylations / Alcohols / Anhydrides / Esters / Zinc perchlorate

A new protocol for the acylation of alcohols with anhydrides in the presence of $Zn(ClO_4)_2 \cdot 6H_2O$ as the catalyst is reported. The activity of $Zn(ClO_4)_2 \cdot 6H_2O$ has been proven to be superior to that exerted by dry $Mg(ClO_4)_2$ and by metal triflates. Its efficiency allows reactions between poorly reactive substrates, such as sterically hindered tertiary alcohols and aromatic anhydrides. All of the reactions were carried out at a 1:1.05 alcohol/anhydride ratio. These conditions are extremely convenient from a practical and economic point of view, since they avoid wasting reagents and allow a simple workup procedure. The catalytic action of $Zn(ClO_4)_2 \cdot 6H_2O$ is so specific for the activation of the anhydrides, that acid-sensitive functionalities and the stereochemical configuration of the starting materials remain unaltered in the esterification process. In all cases, the acylated products are quantitatively obtained in pure form.

Introduction

The acylation of alcohols with anhydrides is an important reaction in organic chemistry. This transformation is, in fact, routinely used during multistep syntheses of natural and specialty products, in both laboratory and industrial processes.[1]

The reaction is sluggish in the absence of an activator. The addition of Lewis bases generally facilitates the process. However, the action of these promoters is efficient only with highly reactive substrates such as primary and secondary alcohols. For instance, the acetylation of tertiary alcohols with DMAP[2] and Bu_3P[3] requires large amounts of catalysts and long reaction times. Therefore, basic catalysis is currently employed only for selected acylations; for example, functionalized DMAP catalysts[4] are useful for the regioselective acetylation of carbohydrates, and optically active phosphanes[5] are efficient for the kinetic resolution of racemic secondary alcohols. The aminophosphane superbases[6] of recent experiments are more efficient, but these compounds show high instability to air moisture.

The acylation reaction is also sensitive to Lewis acid catalysis. Since these promoters strongly increase the electrophilicity of the anhydrides, their action is generally more efficient than the base activation.[7] Therefore, in past years, considerable attention has been devoted to investigating the activity of a large variety of Lewis acids, such as $CoCl_2$,[8] $ZnCl_2$,[9] $TiCl_4/AgClO_4$,[10] Me_3SiCl.[11] More recently, it has been found that metal triflates are highly effective,[12–14] even when loaded in trace amounts. However, triflate catalysis suffers from some drawbacks. For example, the use of $Sc(OTf)_3$[7b] and Me_3SiOTf[12] requires rigorously anhydrous conditions; moreover, in particular circumstances it is necessary to carry out the reaction at low temperatures in order to avoid side reactions. These experimental difficulties have been overcome with the recent discovery that $Bi(OTf)_3$[15] can work with high efficiency even in wet solvents.

More recently, we proposed dried $Mg(ClO_4)_2$ as a useful alternative to metal triflates.[16] This compound, in fact, shows catalytic activity similar to that of $Bi(OTf)_3$, but it does not contain heavy metals, possesses a low molecular weight and is a very low-cost material. These promising results prompted us to study the applications of other perchlorates[17] for the acylation process.

We report now that $Zn(ClO_4)_2 \cdot 6H_2O$ shows strong catalytic activity with results superior to those provided by $Mg(ClO_4)_2$ and metal triflates. It is able to promote acyl-

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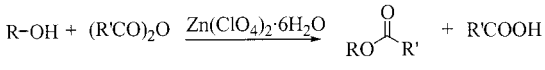
ation of tertiary alcohols with poorly reactive anhydrides acceptably fast. In addition, $Zn(ClO_4)_2·6H_2O$ is stable to air moisture and can work under wet conditions without any loss of efficiency.

Results and Discussion

The main target of this work was to set up a new acylation methodology based on the use of $Zn(ClO_4)_2·6H_2O$ as the catalyst, which could represent an improvement in efficiency and convenience over previously reported procedures.

In this context, the stoichiometric ratio between the reactants has to be considered an important parameter in order to accomplish atom economy, to avoid waste of reagents and to promote green chemistry.[18] In addition, the possibility of working with equimolecular amounts[19] of alcohol and anhydride makes the purification of final products extremely simple. Under the reasonable assumption that the conversion is quantitative, the crude reaction mixture essentially results in a mixture of 1 equiv. of the expected ester and 1 equiv. of the corresponding acid, besides trace amounts of the catalyst (see Scheme 1). A simple treatment with an aqueous $NaHCO_3$ solution is sufficient to completely remove the acid and $Zn(ClO_4)_2·6H_2O$ and to obtain the pure ester.



Scheme 1. Acylation of alcohols with anhydrides in the presence of $Zn(ClO_4)_2·6H_2O$

In the past years, these very convenient conditions had been confined to the special case of highly reactive systems, the common choice being the use of large excesses of the acylating agent. This expedient serves to accelerate the process, avoiding the use of a large amount of the catalyst and/or high reaction temperatures. However, besides implying a waste of the reagent, these conditions result in a troublesome workup procedure due to the necessity of decomposing and removing large amounts of unchanged anhydrides.

Thus, it is clear that the possibility of using equimolecular reagent amounts, even in the case of poorly reactive systems, is closely related to the choice and availability of new and more powerful catalysts.

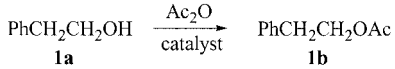
In this context, to test the potential of $Zn(ClO_4)_2·6H_2O$ we analyzed its activity in the acetylation of a primary [2-phenylethanol (**1a**)] and a tertiary alcohol [1-adamantol (**2a**)] with Ac_2O at 20 °C. All of the reactions were monitored by GLC-MS, starting 10 min after the mixing of the reagents.

$Zn(ClO_4)_2·6H_2O$-Catalyzed Acetylation of 2-Phenylethanol (1a) with Ac_2O

The reactions between **1a** (1 equiv.) and Ac_2O (1.05 equiv.) were carried out at 20 °C under solvent-free conditions, since both the alcohol and the anhydride are liquid, and $Zn(ClO_4)_2·6H_2O$ is soluble in Ac_2O.

The process is sluggish in the absence of the catalyst, 8% conversion being observed after 48 h (Table 1, Entry 1).

Table 1. Acetylation of 2-phenylethanol (**1a**) with Ac_2O under solvent-free conditions at 20 °C



Entry	Ac_2O [equiv.]	Catalyst (mol-%)	Time	Yield [%]
1	1.05	none	48 h	8
2	1.05	$Mg(ClO_4)_2$ (1)	10 min	> 99
3	1.05	$Mg(ClO_4)_2$ (0.1)	160 min	> 99
4	1.05	$Zn(ClO_4)_2·6H_2O$ (0.1)	10 min	> 99
5	1.05	$Zn(ClO_4)_2·6H_2O$ (0.05)	30 min	> 99
6	1.05	$Zn(ClO_4)_2·6H_2O$ (0.01)	140 min	> 99
7	10	$Zn(ClO_4)_2·6H_2O$ (0.01)	10 min	> 99
8	10	$Zn(ClO_4)_2·6H_2O$ (0.005)	10 min	> 99

In the presence of 0.1 mol-% of $Zn(ClO_4)_2·6H_2O$, the conversion into the ester is complete in a few minutes (Table 1, Entry 4). Even with smaller amounts of the catalyst (0.05% and 0.01 mol-%), the acetate is quantitatively obtained quite fast (30 min and 140 min, respectively; Table 1, Entries 5 and 6). These findings show that the catalytic activity of $Zn(ClO_4)_2·6H_2O$ is, surprisingly, very high.

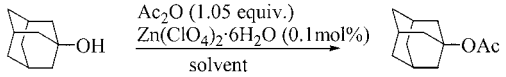
The high potential of $Zn(ClO_4)_2·6H_2O$ emerges from the comparison with other commonly employed Lewis acids. Entries 3 and 4 (Table 1) clearly show that, under the same experimental conditions, $Zn(ClO_4)_2·6H_2O$ is actually more efficient than $Mg(ClO_4)_2$.[16] In fact, the reaction is complete in a few minutes in the presence of 0.1 mol-% of $Zn(ClO_4)_2·6H_2O$, while it goes to completion in 160 min in the presence of 0.1 mol-% of $Mg(ClO_4)_2$. Moreover, it has been reported that 2-phenylethanol can be acetylated at 20 °C within 2.5 h with 10 equiv. of Ac_2O in the presence of 0.005 mol-% of $Bi(OTf)_3$.[7a] Under the same reaction conditions, the use of $Zn(ClO_4)_2·6H_2O$ as the catalyst (Table 1, Entry 8) allows the reaction to go to completion in a few minutes. Since a recent comparative study proved that $Bi(OTf)_3$ is the most active catalyst among metal triflates,[7a] we can conclude that $Zn(ClO_4)_2·6H_2O$ is superior to the more expensive triflates.

$Zn(ClO_4)_2·6H_2O$-Catalyzed Acetylation of 1-Adamantanol (2a) with Ac_2O

Acetylation of tertiary alcohols is considered one of the most difficult transformations due to the large steric hindrance around the tertiary hydroxy group. Therefore, we took 1-adamantanol as a useful probe to test the effective activity of $Zn(ClO_4)_2·6H_2O$.

All of the experiments were carried out at 20 °C by loading the reaction with 0.1 mol-% of $Zn(ClO_4)_2·6H_2O$. Alcohol **2a** is solid at room temperature and requires at least 2 equiv. of Ac_2O to dissolve. With 2 equiv. of Ac_2O, the

Table 2. Acetylation of 1-adamantanol **2a** (1 equiv.) with Ac_2O (1.05 equiv.) in the presence of 0.1 mol-% of $Zn(ClO_4)_2 \cdot 6H_2O$ at 20 °C under various solvent conditions



2a **2b**

Entry	Solvent (equiv.)	Reaction time	Yield (%)
1	–	20 min	> 99[a]
2	–	2 h	> 99
3	AcOH (1)	20 min	> 99
4	AcOH (5)	2.5 h	> 99
5	CH_2Cl_2 (5)	3 h	0
6	THF (5)	5 h	5
7	CH_3CN (5)	5 h	25
8	Et_2O (5)	50 min	> 99
9	Et_2O (10)	3 h	> 99
10	nBu_2O (5)	50 min	> 99

[a] With 2 equiv. of Ac_2O.

acetylation process is complete in a few minutes (Table 2, Entry 1). However, it is possible to carry out the reaction even with only a slight excess of Ac_2O (1.05 equiv.) by adding the alcohol in small portions to the Ac_2O/$Zn(ClO_4)_2 \cdot 6H_2O$ solution; as the reaction proceeds, the solid dissolves in the reaction medium in which AcOH is gradually forming. However, under these conditions, the process is much slower, going to completion within 2 h (Table 2, Entry 2). This result suggests that AcOH can be a suitable solvent for the acetylation reaction. In fact, by adding 1 equiv. of AcOH, the process is complete after 20 min (Table 2, Entry 3). With an excess of 5 equiv. of AcOH, the process becomes slower (Table 2, Entry 4) because, besides a dilution effect, AcOH coordinates the $Zn(ClO_4)_2 \cdot 6H_2O$ with a consequent decrease in its activation effect on Ac_2O.

Since AcOH can be employed as the solvent only in acetylation reactions, we analyzed the effect of other solvents that did not interfere with the anhydride. $Zn(ClO_4)_2 \cdot 6H_2O$ is insoluble in CH_2Cl_2 and, thus, the reaction does not work when using this solvent (Table 2, Entry 5). The reaction is sluggish in THF and CH_3CN; in contrast, it works well in Et_2O (5 equiv.) and nBu_2O (5 equiv.), being complete in 50 min in both cases (Table 2, Entries 8 and 10).

These results demonstrate that trace amounts of $Zn(ClO_4)_2 \cdot 6H_2O$ (0.1 mol-%) are able to activate the acetylation of a poorly reactive tertiary alcohol within a short time, even in the presence of a 1:1 molecular ratio of the reactants.

$Zn(ClO_4)_2 \cdot 6H_2O$-Catalyzed Acetylation of Various Alcohols with Ac_2O

The generality of this acetylation method was explored by testing a large variety of alcohols, under the above-optimized reaction conditions; all of the experiments were carried out by loading the reaction with 0.1 mol-% of $Zn(ClO_4)_2 \cdot 6H_2O$ as the catalyst and with a 1:1.05 alcohol/Ac_2O ratio.

Data reported in Table 3 show that our methodology is general. In fact, the reaction works well not only with primary, secondary and tertiary alcohols, but also with allylic, propargylic and aromatic derivatives.

It is noteworthy that the reaction proceeds in a reasonable time, even with substrates that can capture $Zn(ClO_4)_2 \cdot 6H_2O$ in a chelation process with a consequent decrease in its activation effect on Ac_2O. The α- and β-oxo esters **19a** and **21a**, the α-hydroxy ketone **20a**, the acetonide **25a** and the racemic γ-amino alcohol **26a** are converted into the corresponding acetate in times ranging from 3 to 6 h.

The methodology fails, in part, only in the case of benzylic alcohols. In fact, whereas under solvent-free conditions primary and secondary benzylic substrates can be easily acetylated, the tertiary derivatives **11a** and **12a** undergo an elimination reaction to the corresponding alkenes. No modification of the reaction conditions was successful.

Most of the experiments were carried out under solvent-free conditions. This procedure was adopted even with substrates that were solid at room temperature, such as **6a**, **17a**, **20a**, because, as previously mentioned for 1-adamantanol, as the reaction proceeds, the starting material dissolves. The only exception was **4a**, a highly insoluble long-chain primary alcohol. In this case, it was necessary to carry out the reaction at 40 °C, with an excess of Ac_2O or in the presence of a solvent, such as Et_2O.

The protocol is highly chemoselective. Carbon–carbon double and triple bonds, carbonyl, nitro, dialkylamino, acetonide, bromide, and Me_3Si groups are tolerated.

In all examined cases, the starting material configuration is unaffected by the esterification process; the geometry of carbon–carbon double bonds of homoallylic alcohols remains unaltered (Table 3, Entries 15 and 16). It is well known that homoallylic alcohols can undergo double-bond migration to give the more stable allylic compounds in the presence of trace amounts of acids. As shown in Table 3, Entries 15 and 16, this undesirable isomerization does not occur.

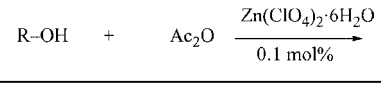
Stereogenic centers do not undergo racemization or epimerization (Table 3, Entries 6, 14, 19, and 21). Among these, the examples reported in Entries 19 and 21 are of particular relevance; these substrates are, in fact, particularly sensitive to acid- or base-promoted racemization, since the stereocenter is in the α-position relative to a carbonyl functional group.

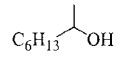
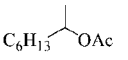
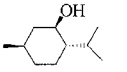
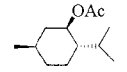
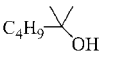
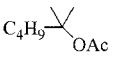
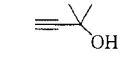
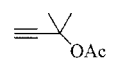
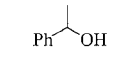
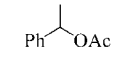
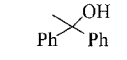
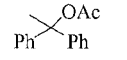
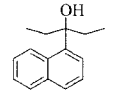
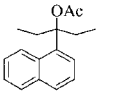
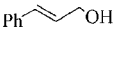
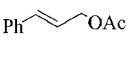
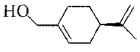
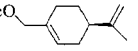
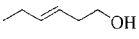
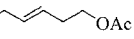
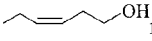
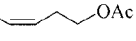
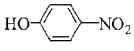
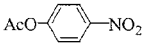
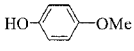
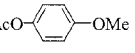
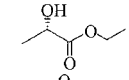
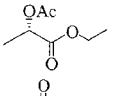
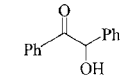
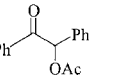
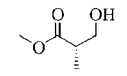
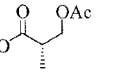
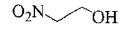
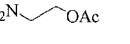
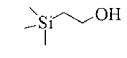
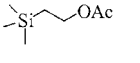
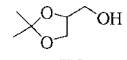
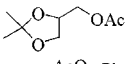
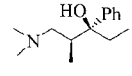
In conclusion, the $Zn(ClO_4)_2 \cdot 6H_2O$ protocol is general and chemoselective, since it allows the conversion of an alcohol into the corresponding acetate without affecting either the geometry of the molecular skeleton, or the structure of a large variety of functional groups present in the substrate.

$Zn(ClO_4)_2 \cdot 6H_2O$-Catalyzed Acylation of Alcohols with Anhydrides

The acylation of alcohols with various anhydrides was also examined. Since we favored the convenience and econ-

Table 3. Acetylation of alcohols (1 equiv.) with Ac_2O (1.05 equiv.) in the presence of 0.1 mol-% of $Zn(ClO_4)_2·6H_2O$ under solvent-free conditions, unless otherwise mentioned



Entry	Substrate		Product		Time	Yield (%)
1	$C_8H_{17}OH$	**3a**	$C_8H_{17}OAc$	**3b**	10 min	> 99
2	$CH_3(CH_2)_{20}CH_2OH$	**4a**	$CH_3(CH_2)_{20}CH_2OAc$	**4b**	3 h[a]	> 99
3	**4a**		**4b**		30 min[b]	> 99
4	**4a**		**4b**		20 min[c]	> 99
5		**5a**		**5b**	10 min	> 99
6		**6a**		**6b**	30 min	> 99
7		**7a**		**7b**	20 min	> 99
8		**8a**		**8b**	1 h	> 99
9	$PhCH_2OH$	**9a**	$PhCH_2OAc$	**9b**	40 min	> 99
10		**10a**		**10b**	10 min	> 99
11		**11a**		**11b**	2 h	0[d]
12		**12a**		**12b**	30 min	0[d]
13		**13a**		**13b**	1 h 50 min	> 99
14		**14a**		**14b**	6 h 30 min	90
15		**15a**		**15b**	1 h	> 99
16		**16a**		**16b**	1 h 50 min	> 99
17		**17a**		**17b**	1 h 50 min	> 99
18		**18a**		**18b**	30 min	> 99
19		**19a**		**19b**	5 h	> 99
20		**20a**		**20b**	6 h	90
21		**21a**		**21b**	4 h 30 min	> 99
22		**22a**		**22b**	10 min	> 99
23	$Br(CH_2)_8CH_2OH$	**23a**	$Br(CH_2)_8CH_2OAc$	**23b**	20 min	> 99
24		**24a**		**24b**	3 h	> 99
25		**25a**		**25b**	5 h	> 99
26		**26a**		**26b**	4 h	95

[a] At reflux, in Et_2O (15 equiv.). [b] At 40 °C, with 5 equiv. of Ac_2O. [c] At 40 °C, with 4 equiv. of AcOH. [d] Only elimination products were recovered.

omical aspects of the methodology, all the reactions were carried out again using a slight excess of anhydride.

When both the anhydride and the alcohol were liquid, the reactions were carried out under solvent-free conditions. However, with poorly reactive anhydrides, it was necessary to increase the temperature and the amount of the catalyst to obtain the esters within an acceptable time. For example, 2-phenylethanol (**1a**) is quantitatively converted into the corresponding propionate **1c** at 20 °C with 0.1 mol-% of $Zn(ClO_4)_2·6H_2O$ in 1 h 20 min (Table 4, Entry 1); under analogous conditions, the reaction of the same alcohol with the less reactive hexanoic anhydride requires 4 h to be completed (Table 4, Entry 2). Vice versa, in order to complete the reaction with pivalic anhydride in a few hours, it is necessary to carry out the reaction at a higher temperatures (40 °C, Table 4, Entry 3). The (*E*)-3-hexenyl alcohol **15a** is less reactive than **1a**; consequently, its acylation with pivalic anhydride required the presence of an increased amount of the catalyst [1 mol-% of $Zn(ClO_4)_2·6H_2O$, Table 4, Entry 9]. Under these conditions, the pivalate is quantitatively formed at 40 °C after 1 h.

When the anhydride and/or the alcohol were solid, acylations were performed in the presence of a solvent, generally Et_2O at reflux. Under these experimental conditions, a significant number of different alcohols can be acylated in the presence of an amount of $Zn(ClO_4)_2·6H_2O$ ranging from 0.1 to 1 mol-%, depending on the reactivity of the starting substrates. For instance, 2-phenylethanol (**1a**) reacts with succinic anhydride in Et_2O at reflux to quantitatively give the corresponding ester after 5 h (Table 4, Entry 5). In an analogous manner, the ester **1f** was obtained by the reaction of **1a** with benzoic anhydride in the presence of 1% of catalyst in Et_2O at reflux for 1 h (Table 4, Entry 4).

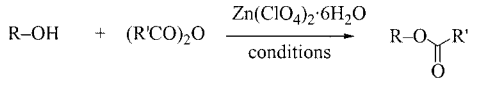
Besides primary alcohols, also secondary and tertiary alcohols can be easily benzoylated at reflux in Et_2O, (Table 4, Entries 7 and 8). Such conversion presents some problems when activated by metal triflates. It has been reported that, in the presence of $Bi(OTf)_3$, tertiary and secondary alcohols do not react or undergo elimination.[7a] Only $Sc(OTf)_3$ is able to allow benzoylation of secondary alcohols, but long reaction times and a large excess of anhydride are required.[7b]

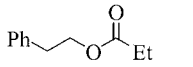
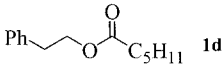
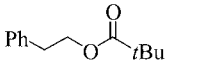
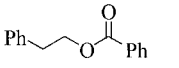
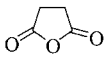
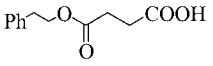
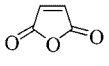
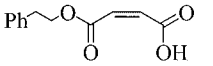
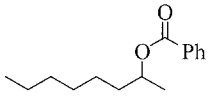
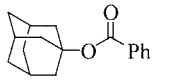
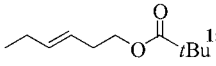
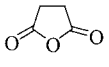
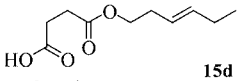
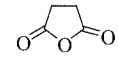
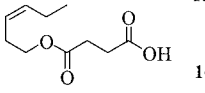
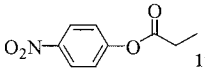
Finally, in all examined cases yields of the desired esters were quantitative, with the exception of the reaction of 2-phenylethanol with maleic anhydride (Table 4, Entry 6) which gave only 75% of the expected monoester **1h**, together with 10 % of the diester, diphenethyl (*Z*)-2-butenedioate. In addition, the formation of a completely insoluble white precipitate was observed, very likely arising from polymerization processes of maleic anhydride.

Conclusion

In this work it has been demonstrated that $Zn(ClO_4)_2·6H_2O$ is a very efficient catalyst for the acylation of alcohols with anhydrides. Its activity has been proved to be superior to that of dry $Mg(ClO_4)_2$ and of metal triflates.

Table 4. Acylation of alcohols (1 equiv.) with anhydrides (1.05 equiv.) in the presence of $Zn(ClO_4)_2 \cdot 6H_2O$ under various reaction conditions



Entry	Substrate	Anhydride	Solvent (equiv.)	Product		% cat.	Time, temp. [°C]	Yield (%)
1	**1a**	$(EtCO)_2O$	–		**1c**	0.1	1 h 15 min, 20°C	> 99
2	**1a**	$(C_5H_{11}CO)_2O$	–		**1d**	0.1	4 h, 20°C	> 99
3	**1a**	$(tBuCO)_2O$	–		**1e**	0.1	3 h, 40°C	> 99
4	**1a**	$(PhCO)_2O$	Et_2O (3)		**1f**	1	1 h, reflux	> 99
5	**1a**		Et_2O (4)		**1g**	0.1	5 h, reflux	> 99
6	**1a**		Et_2O (3)		**1h**	0.1	3.5 h, reflux	75[a]
7	**5a**	$(PhCO)_2O$	Et_2O (3)		**5c**	1	3 h, reflux	> 99
8	**2a**	$(PhCO)_2O$	nBu_2O (3)		**2c**	1	3 h, 70°C	> 99
9	**15a**	$(tBuCO)_2O$	–		**15c**	1	1 h, 40°C	> 99
10	**15a**		Et_2O (3)		**15d**	1	7 h, reflux	> 99
11	**16a**		Et_2O (3)		**16c**	1	7 h, reflux	> 99
12	**17a**	$(EtCO)_2O$	Et_2O (3)		**17c**	1	1 h, reflux	> 99

[a] 10% of the diester, diphenethyl (*Z*)-2-butenedioate, was also recovered.

The efficiency of $Zn(ClO_4)_2 \cdot 6H_2O$ allows for reactions between poorly reactive substrates, such as sterically hindered tertiary alcohols and aromatic anhydrides. In addition, its activity allows it to work at a 1:1.05 alcohol/anhydride ratio, which are extremely convenient conditions from a practical and economic point of view. The catalytic action of $Zn(ClO_4)_2 \cdot 6H_2O$ is so specific for the activation of the anhydrides, that a large variety of acid-sensitive functional groups remain unaltered.

It has been reported that perchlorates can give rise to explosive reactions when heated at high temperatures in the presence of combustible substances.[20] The potential hazard connected with their manufacture and use has prevented their extensive application to industrial processes,[21] especially where large amounts of these compounds are involved. The present work demonstrates that $Zn(ClO_4)_2 \cdot 6H_2O$ is able to act as a powerful promoter even when loaded in trace amounts which begs the question of its use in industrial production. In addition, unlike other perchlorates, there is no need to dry $Zn(ClO_4)_2 \cdot 6H_2O$ at high temperatures, since it works efficiently in its hydrated form.

Experimental Section

General Remarks: Acylating reagents are commercially available and used without purification. All alcohols are commercially available, except **12a**[22] and **26a**.[16] Perchlorates were purchased from Aldrich. All the obtained esters were characterized by ^1H and ^{13}C NMR spectroscopy and the data were compared to those of authentic compounds, both commercially available (**1b**, **3b**, **4b**, **6b**, **8b**, **9b**, **13b**, **15b**, **16b**, **17b**, **20b**, **24b**, **1c**, **2c**, **17c**) or previously reported (**2b**,[23] **5b**,[24] **7b**,[24] **10b**,[25] **14b**,[26] **18b**,[27] **19b**,[28] **22b**,[29] **1d**,[30] **1e**,[31] **1f**,[31] **1g**,[31] **5c**[32]). ^1H NMR experiments were recorded at

300 MHz with a Varian Gemini instrument. ^{13}C NMR and DEPT experiments were acquired at 75 MHz with a Varian Gemini instrument. Chemical shifts are given in ppm from Me_4Si. Coupling constants are given in Hertz (Hz). All the reactions were monitored by GC/MS, starting from 10 min after the mixing of the reagents.

Acetylation of 2-Phenylethanol (1a) with Ac_2O: To a round-bottomed flask were added **1a** (10 mmol) and an acetic anhydride solution of the catalyst (1 mL), prepared from the appropriate amount of the chosen perchlorate and 10 mL of Ac_2O (Table 1, Entries 1−6). In addition, Ac_2O (8.5 mL) was added in the reactions of Entries 7 and 8. The mixture was stirred at 20 °C until the reaction was complete. After Et_2O and aqueous $NaHCO_3$ had been added, the mixture was stirred for 30 min to decompose the excess Ac_2O. The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried with $MgSO_4$ and the solvent was evaporated to give the pure acetate **1b**.

Acetylation of 1-Adamantanol (2a) with Ac_2O: To a round-bottomed flask were added **2a** (10 mmol) and 1 mL of a 10^{-3} M acetic anhydride solution of $Zn(ClO_4)\cdot 6H_2O$ and the calculated amount of the chosen solvent. The mixture was stirred at 20 °C until the reaction was complete. After Et_2O and aqueous $NaHCO_3$ had been added, the mixture was stirred for 30 min to decompose the slight excess of Ac_2O. The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried with $MgSO_4$ and the solvent was evaporated to give the pure acetate **2b**.

$Zn(ClO_4)\cdot 6H_2O$-Catalyzed Acetylation of Alcohols with Ac_2O (General Procedure): The substrate (10 mmol) was added dropwise when liquid, or in small portions when solid, to 1 mL of a 10^{-3} M acetic anhydride solution of $Zn(ClO_4)\cdot 6H_2O$. The mixture was stirred at 20 °C until the reaction was complete. After Et_2O and aqueous $NaHCO_3$ had been added, the mixture was stirred for 30 min to decompose the slight excess of Ac_2O. The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried with $MgSO_4$ and the solvent was evaporated to give the pure acetates.

$Zn(ClO_4)\cdot 6H_2O$-Catalyzed Acylation of Alcohols with Anhydrides (Representative Procedure): To a round-bottomed flask were added 2-phenylethanol (**1a**) (1.22 g, 10 mmol), $Zn(ClO_4)\cdot 6H_2O$ (37 mg, 0.1 mmol), benzoic anhydride (2.38 g, 10.5 mmol) and Et_2O (3.15 mL, 30 mmol). The mixture was heated at reflux for 1 h, and then cooled to room temperature. After Et_2O and aqueous $NaHCO_3$ had been added, the mixture was stirred for 30 min to decompose the slight excess of $(PhCO)_2O$. The aqueous layer was separated and extracted with Et_2O. The combined organic layers were dried with $MgSO_4$ and the solvent was evaporated to give the pure ester **1f** (2.25 g, yield > 99 %). Spectroscopic data of compounds not found in the literature:

Methyl (2*S*)-3-(Acetyloxy)-2-methylpropanoate (21b): Yield > 99 %, 0.64 g starting from (0.47 g, 4 mmol) of **21a**. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ = 1.21 (d, 3 H, CH_3, $J_{H,H}$ = 7.2), 2.05 (s, 3 H, CH_3), 2.70−2.90 (m, 1 H, CH), 3.71 (s, 3 H, CH_3), 4.13 (dd, 1 H, CH_2, $J_{H,H}$ = 10.7, $J_{H,H}$ = 5.7), 4.20 (dd, 1 H, CH_2, $J_{H,H}$ = 10.7, $J_{H,H}$ = 7.2). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 13.5 (CH_3), 20.5 (CH_3), 38.7 (CH_3), 51.6 (CH), 65.2 (CH_2), 170.4 (C), 174.0 (C).

9-Bromononyl Acetate (23b): Yield > 99 %, 0.53 g starting from (0.45 g, 2 mmol) of **23a**. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ = 1.35−1.50 (m, 10 H, CH_2), 1.50−1.70 (m, 2 H, CH_2), 1.75−1.95 (m, 2 H, CH_2), 2.05 (s, 3 H, CH_3), 3.41 (t, 2 H, CH_2, $J_{H,H}$ = 6.8), 4.05 (t, 2 H, CH_2, $J_{H,H}$ = 6.7). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 20.9 (CH_3), 25.8 (CH_2), 28.0 (CH_2), 28.5 (CH_2), 28.6 (CH_2), 29.0 (CH_2), 29.2 (CH_2), 32.7 (CH_2), 33.9 (CH_2), 64.5 (CH_2), 171.1 (C).

(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl Acetate (25b): Yield > 99 %, 1.73 g starting from (1.32 g, 10 mmol) of **25a**. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ = 1.31 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 3.60−3.75 (m, 1 H), 3.95−4.15 (m, 3 H), 4.20−4.35 (m, 1 H). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 20.7 (CH_3), 25.3 (CH_3), 26.6 (CH_3), 64.8 (CH_2), 66.2 (CH_2), 73.5 (CH), 109.8 (C), 170.8 (C).

(1*SR*,2*SR*)-3-(Dimethylamino)-1-ethyl-2-methyl-1-phenylpropyl Acetate (26b): Yield 95 %, 0.25 g starting from (0.22 g, 1 mmol) of **26a**. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ = 0.72 (t, 3 H, CH_3, $J_{H,H}$ = 7.2), 0.78 (d, 3 H, CH_3, $J_{H,H}$ = 7.1), 1.55−1.70 (m, 1 H), 1.95−2.05 (m, 1 H), 2.09 (s, 3 H, CH_3), 2.11 (s, 6 H, $2CH_3$), 2.45−2.70 (m, 3 H), 7.15−7.30 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 8.0 (CH_3), 13.5 (CH_3), 22.1 (CH), 26.8 (CH_2), 37.4 (CH_3), 45.9 (CH_3), 62.6 (CH_2), 90.0 (C), 126.3 (CH), 126.8 (CH), 127.5 (CH), 140.0 (C), 169.8 (C).

(*Z*)-4-Oxo-4-(phenethyloxy)-2-butenoic Acid (1h): Yield 75 %, 1.65 g starting from (1.22 g, 10 mmol) of **1a**. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ = 3.02 (t, 2 H, CH_2, $J_{H,H}$ = 7.4), 4.48 (t, 2 H, CH_2, $J_{H,H}$ = 7.4), 6.35 (d, 1 H, CH, $J_{H,H}$ = 12.6), 6.43 (d, 1 H, CH, $J_{H,H}$ = 12.6), 7.20−7.40 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 34.5 (CH_2), 66.7 (CH_2), 126.7 (CH), 128.5 (CH), 128.7 (CH), 130.0 (CH), 133.7 (CH), 136.8 (C), 166.2 (C), 166.8 (C).

(*E*)-3-Hexenyl Pivalate (15c): Yield > 99 %, 1.83 g starting from (1.00 g, 10 mmol) of **15a**. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ = 0.95 (t, 3 H, CH_3, $J_{H,H}$ = 7.4), 1.19 (s, 9 H, $3CH_3$), 1.90−2.05 (m, 2 H, CH_2), 2.35−2.45 (m, 2 H, CH_2), 4.05 (t, 2 H, CH_2, $J_{H,H}$ = 6.7), 5.30−5.40 (m, 1 H, CH), 5.45−5.60 (m, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 13.7 (CH_3), 25.6 (CH_2), 27.2 (CH_3), 32.0 (CH_2), 38.7 (C), 63.8 (CH_2), 124.2 (CH), 134.9 (CH), 178.6 (C).

4-[(*E*)-3-Hexenyloxy]-4-oxobutanoic Acid (15d): Yield > 99 %, 1.99 g starting from (1.00 g, 10 mmol) of **15a**. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ = 0.94 (t, 3 H, CH_3, $J_{H,H}$ = 7.5), 1.90−2.05 (m, 2 H, CH_2), 2.20−2.35 (m, 2 H, CH_2), 2.55−2.65 (m, 4 H, 2 CH_2), 4.05−4.10 (m, 2 H, CH_2), 5.25−5.40 (m, 1 H, CH), 5.45−5.65 (m, 1 H, CH), 7.9 (br. s, 1 H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 13.7 (CH_3), 25.5 (CH_2), 28.8 (CH_2), 28.9 (CH_2), 31.8 (CH_2), 64.4 (CH_2), 123.8 (CH), 135.2 (CH), 172.1 (C), 177.7 (C).

4-[(*Z*)-3-Hexenyloxy]-4-oxobutanoic Acid (16c): Yield > 99 %, 1.99 g starting from (1.00 g, 10 mmol) of **16a**. ^1H NMR ($CDCl_3$, 300 MHz, ppm): δ = 0.94 (t, 3 H, CH_3, $J_{H,H}$ = 7.5), 1.95−2.10 (m, 2 H, CH_2), 2.30−2.40 (m, 2 H, CH_2), 2.55−2.70 (m, 4 H, 2 CH_2), 4.00−4.10 (m, 2 H, CH_2), 5.20−5.35 (m, 1 H, CH), 5.45−5.55 (m, 1 H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz, ppm): δ = 14.1 (CH_3), 20.5 (CH_2), 26.6 (CH_2), 28.7 (CH_2), 28.9 (CH_2), 64.3 (CH_2), 123.4 (CH), 134.6 (CH), 172.1 (C), 178.2 (C).

Acknowledgments

Work carried out in the framework of the National Project "Stereoselezione in Sintesi Organica, Metodologie e Applicazioni" supported by MIUR, Rome, and by the University of Bologna, in the framework of "Progetto di Finanziamento Pluriennale, Ateneo di Bologna".

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Received July 24, 2003

