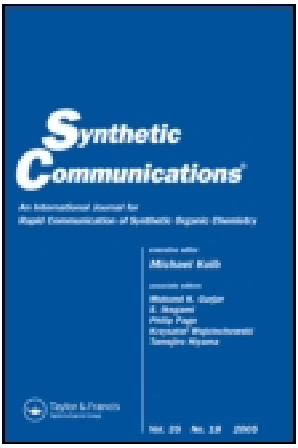

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Microwave-Assisted $NiCl_2$ Promoted Acylation of Alcohols

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Microwave-Assisted $NiCl_2$ Promoted Acylation of Alcohols

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ABSTRACT

A microwave oven acylation of alcohols by carboxylic acid anhydrides has been developed. $NiCl_2$ has been proven an efficient catalyst for the acylation of primary, secondary, and tertiary alcohols and phenols under microwave conditions.

Key Words: Acetylation; Acylation; Microwave; Metal catalysis.

Acylation of alcohols is one of the most frequently used transformations in organic synthesis presenting both academic as well as industrial interest. Acid anhydrides have been proven the most useful reagents for the reaction

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in the presence of base or acid catalysts.[1] 4-(Dimethylamino)pyridine (DMAP) is the most popular among the nucleophilic catalysts catalyzing the acylation of alcohols at enhanced rate.[2,3] Besides the nucleophilic catalysts, a number of acidic catalysts have been studied so far. A variety of Lewis acids such as $ZnCl_2$,[4] $CoCl_2$,[5] and in particular metal triflates such as $Sc(OTf)_3$,[6] $Bi(OTf)_2$,[7] $Cu(OTf)_2$,[8] and $Sn(OTf)_2$[8] have been found to be effective catalysts for acylation. During the past decade, the interest in microwave-assisted organic synthesis has increased significantly.[9−11] Most recently, the microwave oven synthesis of esters promoted by imidazole has been reported.[12] In the present article, we describe our studies on the microwave assisted acylation of alcohols in the presence of $NiCl_2$ as promoter.

A common microwave oven was used for the experiments and the reaction mixture each time was irradiated at 600 W. The results obtained for the acylation of benzyl alcohol under various conditions are presented in Table 1. When a mixture of benzyl alcohol and acetic anhydride in the absence of any catalyst was irradiated for 7 min in 1 : 2 and 1 : 1 molar ratio, benzyl acetate was isolated in 66% and 50% yield, respectively. However, in the presence of 5% $NiCl_2 \cdot 6H_2O$ the yield of the reaction was 100% and 70%, when the molar ratio was 1 : 2 and 1 : 1, respectively. In the absence of any catalyst and when the ratio of benzyl alcohol and acetic anhydride was 1 : 2, the product was obtained quantitatively after 14 min under irradiation. Similar results were obtained when $CoCl_2 \cdot 6H_2O$ instead of $NiCl_2 \cdot 6H_2O$. Because $NiCl_2 \cdot 6H_2O$ is cheaper than $CoCl_2 \cdot 6H_2O$, the acylation reaction was studied by using $NiCl_2 \cdot 6H_2O$ as a catalyst. Direct acetylation of benzyl alcohol by acetic acid under microwave irradiation and in the presence of $NiCl_2 \cdot 6H_2O$ led to low yields. Even when the acetylating agent was used in excess (alcohol : acid 1 : 15), benzyl

Table 1. Acylation of benzyl alcohol under microwave irradiation.

Acylating agent	Benzyl alcohol : acylating agent ratio	Catalyst	Time (min)	Yield (%)
$(CH_3CO)_2O$	1 : 2	—	7	66
$(CH_3CO)_2O$	1 : 1	—	7	50
$(CH_3CO)_2O$	1 : 2	—	14	98
$(CH_3CO)_2O$	1 : 2	$NiCl_2 \cdot 6H_2O$	7	100
$(CH_3CO)_2O$	1 : 1	$NiCl_2 \cdot 6H_2O$	7	70
$(CH_3CO)_2O$	1 : 2	$CoCl_2 \cdot 6H_2O$	7	100
$(CH_3CO)_2O$	1 : 1	$CoCl_2 \cdot 6H_2O$	7	70
CH_3COOH	1 : 15	$NiCl_2 \cdot 6H_2O$	12	21
$(CH_3CH_2CO)_2O$	1 : 2	$NiCl_2 \cdot 6H_2O$	8	67

acetate was isolated in 21% yield after 12 min in the microwave oven, under reflux. Furthermore, benzyl propionate was isolated in high yield when a mixture of benzyl alcohol and propionic anhydride (1 : 2) was irradiated in the presence of $NiCl_2 \cdot 6H_2O$.

The above results indicate that $NiCl_2$ is an efficient catalyst for the microwave assisted acylation of benzyl alcohol. To explore the scope and the limitations of the method, a variety of primary, secondary, and tertiary alcohols and phenols were acetylated by acetic anhydride in a microwave oven using $NiCl_2$ as the catalyst. The results are summarized in Table 2.

Esters of primary alcohols such as p-methoxybenzyl alcohol (entry 1), o-and p-nitrobenzyl alcohol (entry 2 and 3), 3-phenylpropanol (entry 4), geraniol (entry 5), nerol (entry 6) were isolated in high to excellent yields. Acetylation of citronellol (entry 7) was accomplished in a moderate yield. Acetylated phenol was isolated in quantitative yield (entry 8), whereas thymol (entry 9) and 3-hydroxybenzaldehyde (entry 10) were acetylated in 78% and 60% yield, respectively, after irradiation for 10 and 12 min.

When our protocol was applied to secondary alcohols such as cyclohexanol (entry 11) and borneol (entry 12), the desired acetates were obtained in 80% and 68%, respectively. Acetylation of 1,2-hexanediol (entry 13) using a 1 : 1 ratio of acetic anhydride per hydroxyl group for 14 min led to a mixture 7 : 3 of diacetylated : monoacetylated compound. Increasing the ratio to 1 : 1.5 per hydroxyl group the diacetylated compound was isolated in 88% yield.

Tertiary alcohols (entries 15 and 16) were esterified in low yields (20 and 14%, respectively).

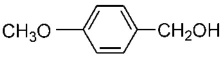
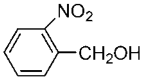
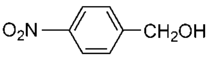
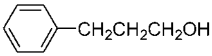
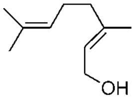
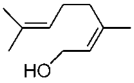
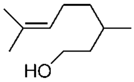
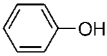
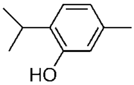
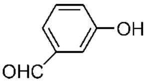
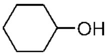
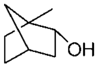
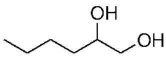
All the products are known compounds and are easily identified by comparison of their physical properties with those of authentic samples.

In conclusion, our esterification method under microwave conditions in the presence of $NiCl_2$ can be readily applied to a variety of alcohols (primary, secondary, and tertiary) and phenols. The microwave-assisted acetylation has the benefit of reducing reaction times in comparison with acetylation under conventional conditions. The advantages of the present method in terms of fast reaction rates and ease of manipulation should make this protocol a valuable alternative to the existing methods.

TYPICAL EXPERIMENTAL PROCEDURE

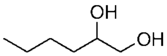
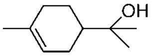
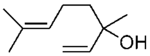
In a typical experiment the mixture of alcohol and acetic anhydride (1 : 2) was irradiated in the microwave oven at 600 W for 7–12 min in the presence of 5% $NiCl_2 \cdot 6H_2O$. The reaction mixture was extracted with ethyl acetate or ether and the organic layer was washed with H_2O, 10% $NaHCO_3$ and brine and was dried over $MgSO_4$. The solvent was evaporated, and the residue was

Table 2. Esterification of alcohols with acetic anhydride in the presence of $NiCl_2$.

Entry	Alcohol : Ac_2O	Alcohol	Time (min)	Yield (%)
1	1 : 2		7	98
2	1 : 2		8	90
3	1 : 2		10	90
4	1 : 2		7	98
5	1 : 2		8	83
6	1 : 2		8	87
7	1 : 2		8	62
8	1 : 2		10	96
9	1 : 2		10	78
10	1 : 2		12	60
11	1 : 2		10	80
12	1 : 2		10	68
13	1 : 2		14	70[a] : 30[b]

(*continued*)

Table 2. Continued.

Entry	Alcohol : Ac_2O	Alcohol	Time (min)	Yield (%)
14	1 : 3		10	88
15	1 : 2		12	20
16	1 : 2		12	14

[a] Diacetylated compound.
[b] Acetylation of the primary hydroxy group only.

purified by column chromatography by using petroleum ether : ether 8 : 2 as eluent.

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