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Note

Protection of aldehydes as 1,1-diacetates and deprotection of 1,1-diacetates to aldehydes

Puja Nanda, Satya Paul & Rajive Gupta*

Department of Chemistry, University of Jammu
Jammu 180 006, India

Email: rajgupta@sancharnet.in

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Protection of aldehydes as 1,1-diacetates using Ac_2O/acidic alumina and deprotection of 1,1-diacetates to aldehydes using acidic alumina has been reported by microwave irradiation. Selective protection in the case of 4-hydroxybenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde and deprotection in the case of 4-acetoxybenzaldehyde diacetate are described.

Keywords: Protection, deprotection, aldehydes, acidic alumina, environment-friendly, microwave activation

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One of the important strategies in devising organic synthesis is the protection and deprotection of functional groups. Selective protection and deprotection of carbonyl group represent an important role in multi-step synthesis of complex natural products[1]. Protection of aldehydes as 1,1-diacetates is an important transformation due to its moderately stable nature[2] and ease of preparation. These are also important precursors[3] for the synthesis of acetoxy dienes and dihalovinyl acetates. Acylals are useful as cross-linking reagents[4] for cellulose in cotton and serve as activators[5] in the composition of bleaching mixture used for the treatment of wine strained fabrics.

Generally, the protection of aldehydes as 1,1-diacetates was carried out in the presence of strong acids such as sulfuric acid[6], phosphoric acid or methane sulfonic acid[7] and lewis acids such as $FeCl_3$ (ref. 8) and PCl_3 (ref. 9). Beta zeolite[10], montmorillonite KSF[11], iodine[12], graphite[13], ferrous sulphate[14], amberlyst-15 (ref. 15), envirocat EPZG[16], HSZ-360 (ref. 17), sulfated zirconia[18], poly(vinylchloride)/ $FeCl_3$ (ref. 19) and indium chloride[20] have also been used for the protection of aldehydes as 1,1-diacetates.

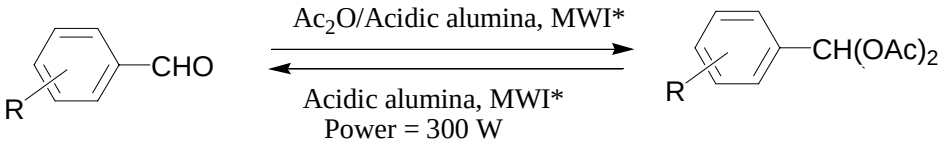
Further, deprotection of 1,1-diacetates to aldehydes is equally important as after protection, the next step is deprotection. Numerous reagents/catalysts are available for the deprotection of 1,1-diacetates to aldehydes such as alcoholic sulfuric acid[21], sodium hydroxide or potassium carbonate[2], boron triiodide-*N*,*N*-diethylaniline complex[22], ceric ammonium nitrate over silica gel[23], montmorillonite K10 (ref. 24), graphite[25], scandium triflate[26], $CeCl_3.7H_2O$-NaI system[27], bismuth(III)chloride[28,] indium chloride[20], and TiO_2/SO_4^{2-} (ref. 29).

Many reagents for the protection of aldehydes as 1,1-diacetates and deprotection of 1,1-diacetates were reported under microwave irradiation. Some of the reagents used for the protection of aldehydes as 1,1-diacetates are montmorillonite K10 (ref. 30), envirocat EPZ 10® (ref. 31) and $SiO_2/FeCl_3$[32], neutral alumina[33], montmorillonite K10 (ref. 34), KSF[35], envirocat EPZG® [36], Y zeolite HSZ-360 (ref. 17) and alumina[37] were described for the deprotection of 1,1-diacetates to aldehydes. However, many of these methods involve strongly acidic or oxidizing conditions, expensive and hazardous reagents, long reaction times, low yields, involve use of solvents and may affect other functional groups.

Microwave irradiation for organic reactions has rapidly gained popularity as it accelerates a variety of synthetic transformations[38]. Reactions that are facilitated by supported reagents on various solid inorganic surfaces have received attention in recent years[39]. The advantages of these methods over conventional heating are that they provide greater selectivity, enhanced reaction rates and cleaner products.

In continuation of our ongoing program to develop environmentally benign methods using solid supports[40], herein, we report an efficient, rapid, economic and environment-friendly method for the preparation and cleavage of 1,1-diacetates using acetic anhydride adsorbed on acidic alumina and acidic alumina, respectively. The support can be re-used several times without loss of activity after simple washing with suitable solvents.

Aldehydes of different types were protected by using acetic anhydride adsorbed on acidic alumina. The corresponding diacetates were obtained in moderate to excellent yields. However, deprotection of 1,1-diacetates can be carried out by irradiating



Scheme I

Table I—Protection of aldehydes as 1,1-diacetates using Ac_2O/acidic alumina and deprotection of 1,1-diacetates to aldehydes using acidic alumina under MW irradiation (Power = 300 W)

Entry	Substrate for protection/ Deprotection product	Substrate for deprotection/ Protection product	Protection[a]		Deprotection[a]	
			Time (min)	Yield[b] (%)	Time (min)	Yield[a] (%)
1	Benzaldehyde	Acetyloxyphenylmethyl acetate	3	99	7	96
2	Cinnamaldehyde	(2*E*)-1-Acetyloxy-3-phenylprop-2-ene-1-acetate	4	70	6	76
3	Anisaldehyde	Acetyloxy(4-methoxyphenyl)methyl acetate	3	70	6	74
4	4-Hydroxybenzaldehye	Acetyloxy(4-hydroxyphenyl)methyl acetate[c]	10	72	6	79
5	4-Nitrobenzaldehyde	Acetyloxy(4-nitrophenyl)methyl acetate	8	83	4	84
6	3-Nitrobenzaldehyde	Acetyloxy(3-nitrophenyl)methyl acetate	6	80	4	82
7	Furfural	Acetyloxy-2-furylmethyl acetate	10	62	8	72
8	4-Chlorobenzaldehyde	Acetyloxy(4-chlorophenyl)methyl acetate	7	71	5	70
9	4-Hydroxy-3-methoxy-benzaldehyde	Acetyloxy(4-hydroxy-3-methoxyphenyl)methyl acetate	9	81	5	84
10	4-Acetyloxybenzaldehyde[d]	Acetyloxy(4-acetyloxyphenyl)methyl acetate	8	70	7	74

[a]Protection: formation of 1, 1-diacetates from aldehydes; Deprotection: cleavage of 1, 1-diacetates to aldehydes.
[b]Isolated yield from three experimental runs.
[c]Selectively acetyloxy(4-hydroxyphenyl)methyl acetate was obtained as the protection product.
[d]Selectively 4-acetyloxybenzaldehyde was obtained as the deprotection product.

1,1-diacetates using acidic alumina as support under microwave irradiation (**Scheme I**, **Table I**).

It is noteworthy that acetic anhydride when adsorbed over basic alumina was found to act as an efficient reagent for the formation of 1,1-diacetate in case of benzaldehyde, 4-chlorobenzaldehyde and 4-methoxybenzaldehyde but failed for 4-hydroxy-benzaldehyde where acetylation of 4-hydroxy group takes place. However, when acidic alumina was used as support instead of basic alumina, various substituted aromatic aldehydes were converted to their corresponding 1,1-diacetates in moderate to excellent yields. In the case of 4-hydroxybenzaldehyde and 4-hydroxy-3-methoxybenzaldehyde (entry 4 and 9, **Table I**), only -CHO group gets converted to -$CH(OAc)_2$ whereas, -OH group remains unaffected. The reagent also worked well for the protection of cinnamaldehyde and furfural. It is interesting to mention here that acidic alumina was found to be highly efficient support under MW irradiation for the deprotection of 1,1-diacetates of aldehydes. The results are summarized in **Table I**. In the case of acetyloxy(4-acetyloxyphenyl)methyl acetate (entry 10, **Table I**), only $–CH(OAc)_2$ group gets converted to –CHO group, whereas –OAc group remains unaffected. Thus, this method could be used for the selective deprotection of $–CH(OAc)_2$ to –CHO group when –OAc group is also present together.

The structures of the products were confirmed by ^{1}H NMR, IR and mass spectral data and by comparison with authentic samples.

Experimental Section

General. Melting points were determined on a Buchi melting point apparatus and are uncorrected. ^{1}H NMR spectras were recorded on a JNM-PMX 60 NMR spectrometer (60MHz) in $CDCl_3$ using tetramethylsilane as internal standard; and IR spectras in KBr disc on a Hitachi 270-30 spectrophotometer. The reactions were monitored by TLC. For the microwave irradiation experiments described below, a conventional (unmodified) household microwave oven was used (BPL BMO 800, 800 W and operating at 2450 MHz).

Protection of aldehydes as 1,1-diacetates using Ac_2O/acidic alumina. General procedure. To a mixture of the aromatic aldehyde (2 mmoles) and acetic anhydride (4 mmoles) in a 50 mL borosil beaker, 3g of acidic alumina was added. The reaction mixture was stirred thoroughly (30 s) till free flowing powder was obtained and irradiated in the microwave oven for an appropriate time (**Table I**) at 300 W (monitored by TLC). On cooling at room temperature, the product was extracted with methylene chloride (3×15 mL). The combined methylene extracts were washed with water and dried over anhydrous sodium sulphate. The product obtained after removal of the solvent under reduced pressure was crystallized from pet. ether-ethyl acetate.

Deprotection of 1,1-diacetates to aldehydes using acidic alumina. General procedure. To appropriate 1,1-diacetate (1 mmole) in a borosil beaker (50 mL), 1g of acidic alumina was added. The mixture was stirred thoroughly till free flowing powder was obtained and irradiated in the microwave oven for an appropriate time (**Table I**) at 300 W (monitored by TLC). On cooling at room temperature, the product was extracted with methylene chloride (3×15mL). The combined methylene extracts were washed with water and dried over anhydrous sodium sulphate. The product obtained after removal of the solvent under reduced pressure was crystallized from ethyl acetate.

Conclusion

A simple, rapid, solvent-free, inexpensive and environment-friendly procedure has been developed for the protection of aldehydes as 1,1-diacetates and deprotection of 1,1-diacetates under microwave heating which can be a useful alternative to existing methods.

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