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Rapid and Efficient Method for the Synthesis of Acylals from Aldehydes and Their Deprotection Catalyzed by *p*-Toluene Sulphonic Acid (*p*-TSA)

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Abstract: A simple, rapid, and efficient method has been developed for the synthesis of acylals from aldehydes using acetic anhydride in the presence of a catalytic amount *p*-TSA at 25°C, and the deprotection of acylals using water and catalytic *p*-TSA under microwave irradiation has been achieved in excellent yields.

Keywords: acylals, aldehydes, microwave irradiation, *p*-TSA, solvent-free condition

Selective protection and deprotection of carbonyl groups are of great importance in synthetic organic chemistry. In the past decade, 1,1-diacetates have received increasing attention, because these compounds are precursors[1] for synthetically useful acetoxy dienes and di-halovinyl acetates. In addition, acylals are useful in the nucleophilic substitution reactions.[2] Furthermore, 1,1-diacetates have been applied as cross-linking reagents for cellulose in cotton and serve as activators in the composition of the bleaching mixture used for the treatment of wire-strained fabrics.[3] The preparation of acylals were carried out using several catalysts such as protic[4] or Lewis acids,[5] iodine,[6] NBS,[7] and metal salts such as $LiBF_4$,[8a] $AlPW_{12}O_{40}$,[8b] $Bi(NO_3)_3 \cdot 5H_2O$,[8c] $Bi(OTf)_3 \cdot xH_2O$ or Li(OTf),[8d] and $H_6P_2W_{18}O_{62} \cdot 24H_2O$.[8e] In addition, montmorillonite K-10[9] and

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zeolites[10] have been used for the purpose. Even though methods have been developed for the protection of aldehydes as their diacetates, a limited number of methods are available for deprotection of 1,1-diacetates to aldehydes. Use of strong acids such as sulfuric acid or hydrochloric acid,[11] boron-tri-iodide-*N,N*-diethyl aniline complex,[12] TiO_2/SO_4,[13] montmorillonite clay,[14] neutral alumina,[15] and recently graphite [16] and $AlCl_3$[17] has been documented in the literature for the deprotection of 1,1-diacetates. However, none of these methods claimed to give protection as well as deprotection except zeolite Y,[18] zirconium sulfophenyl phosphonate,[19] and ceric ammonium nitrate.[20] The reported methods entail low yields, long reaction times, corrosivity, and difficult workup and require thermal activation before use. The reactions are carried out in harmful chlorinated solvents and expensive reagents and demand an inert atmosphere.

In continuation of our research on solvent-free and microwave irradiation reactions,[21] herein we report a rapid and efficient method for the synthesis of acylals from aldehydes and acetic anhydride under solvent-free condition at 25°C and regeneration of aldehydes in aqueous CH_3CN from the respective 1,1-diacetates under microwave irradiation using a catalytic amount of inexpensive and readily available *p*-TSA within a minute in excellent yields (Scheme 1).

To optimize the reaction conditions, initially we tried to convert benzaldehyde (1 mmol) to the corresponding acylals with *p*-TSA (0.1 mmol) and acetic anhydride (2 mmol) in the presence of various solvents and also under solvent-free condition. As shown in Table 1, in comparison to conventional methods, the yield of the products under solvent-free conditions is greater and the reaction time is much less. Therefore, we employed solvent-free conditions for conversion of various aldehydes to the corresponding acylals (Table 2).

By using this catalyst, aldehydes having electron-releasing or electron-withdrawing groups were converted to their corresponding diacetates in excellent yields within a minute. Moreover, the protocol could also work with α,ß-unsaturated aldehydes (Table 2, Entry 6). Ketones such as acetophenone and benzophenone did not give any acylals under the reaction conditions even after 24 h (Table 2, entries 9 and 10).

As mentioned in the introduction, it is very important to selectively protect the aldehyde moiety in the presence of a kenotic carbonyl group. We reacted an equimolecular mixture of benzophenone and benzaldehyde with a twofold excess of acetic acid in the presence of *p*-TSA, and the

$$\text{R-CHO} \underset{\text{p-TSA, H}_2\text{O in CH}_3\text{CN, MW}}{\overset{\text{Ac}_2\text{O, p-TSA, 25}^0\text{C}}{\rightleftarrows}} \text{RCH(OAc)}_2$$

Scheme 1.

Table 1. Conversion of benzaldehyde (1 mmol) to 1,1-diacetoxy-1-phenylmethane in different solvents and under solvent-free conditions in the presence of *p*-TSA (0.1 mmol)[a]

Entry	Solvent[b]	Yield (%)[c]	Time (min)
1	CH_2Cl_2	88	10
2	MeCN	75	10
3	EtOAc	60	15
4	Et_2O	65	15
5	Toluene	80	10
6	Solvent free	94	40 s

[a] Reaction was conducted by stirring with 2 mmol of Ac_2O at room temperature.
[b] Reaction was carried out in 5 mL of solvent at room temperature.
[c] Yields refer to isolated pure products.

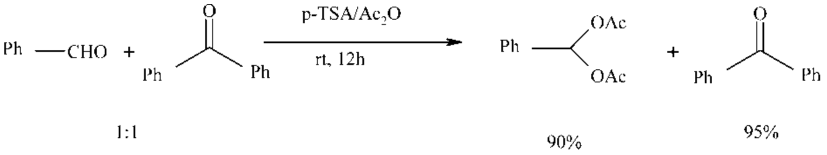
reaction mixture was worked up (after 12 h) to give the benzaldehyde 1,1-diacetate (90% yield) and recover the unchanged benzophenone (Scheme 2).

We next investigated the use of catalyst in the deprotection of acylals to the corresponding aldehydes by treatment of acylals using a catalytic amount of *p*-TSA in the presence of water–acetonitrile (1:1) under microwave irradiation and found that a power level of 320 W is the most suitable one for the reaction. By this method, aromatic and α,ß-unsaturated acylals

Table 2. Diacetoxylation of aldehydes using acetic anhydride in the presence of catalytic *p*-TSA under solvent-free condition at 25°C

Entry	Substrate (s)	Reaction time (%)	Yield[a]	Mp (°C) Found	Mp (°C) Reported
1	Benzaldehyde	25	96	43–44	44–45[4b]
2	*m*-Nitrobenzaldehyde	45	89	103–105	65–66[5c]
3	*p*-Nitrobenzaldehyde	40	92	123–126	125–127[4b]
4	*m*- Chlorobenzaldehyde	30	85	63–64	64–65[5c]
5	2-Furaldehyde	35	90	50–51	52–53[4b]
6	Cinnamaldehyde	35	92	83–85	84–87[9]
7	*p*-Methoxybenzaldehyde	30	90	62–64	64–65[9]
8	Vanillin	30	80	89–91	90–91[4b]
9	Acetophenone	24 h	ND		
10	Benzophenone	24 h	ND		

[a] ND: not detected.



Scheme 2.

have been transformed into the corresponding aldehydes in high yields (Table 3).

A plausible mechanism of the *p*-TSA catalyzed reaction is shown in Scheme 3.

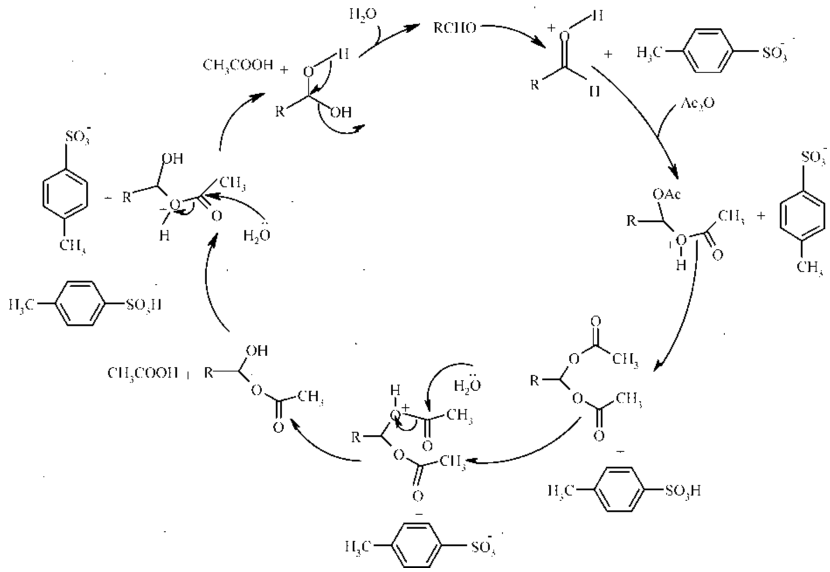
In conclusion, we have developed a rapid and efficient method for the preparation of acylals from aldehydes using acetic anhydride in the presence of a catalytic amount of inexpensive and readily available *p*-TSA without using any solvent at 25°C, and we have also demonstrated that the diacetates can be deprotected to the corresponding aldehydes using a catalytic amount of *p*-TSA and water–acetonitrile under microwave irradiation in excellent yields within a minute.

Table 3. Deprotection of acylals in the presence of catalytic *p*-TSA and 1:1 H_2O-CH_3CN under microwave irradiation

Entry	Substrate	Reaction time (s)	Yield (%)	Bp (torr) or mp (°C)	
				Found	Reported
1	1,1-Diacetoxy-1-phenyl methane	25	94	179–180	180–183[a]
2	1,1-Diacetoxy-1-(3-nitrophenyl)methane	30	80	56–57	57–59[a]
3	1,1-Diacetoxy-1-(4-nitrophenyl)methane	35	82	103–105	104–106[b]
4	1,1-Diacetoxy-1-(3-chlorophenyl)methane	40	75	63–64	213–214[a]
5	1,1-Diacetoxy-1-(2-furyl)methane	35	78	160–162	161–163[a]
6	1,1-Diacetoxy-3-phenyl-prop-2-ene	30	80	242–245	248[b]
7	1,1-Diacetoxy-1-(4-methoxyphenyl)methane	30	82	115–117	118–120[a]
8	1,1-Diacetoxy-1-(4-hydroxy-3-methoxyphenyl)-methane	30	75	80–81	81–83[b]

[a] Aldrich Handbook of Fine Chemicals.

[b] Lancaster Research Chemicals, 2002–2003.



Scheme 3.

EXPERIMENTAL

All aldehydes, *p*-TSA, and solvents are purchased from BDH/Merck, s.d. fine chemicals, and all the aldehydes and solvents were distilled before use. Synthesis and deprotection of 1,1-diacetates were carried out at room temperature using a conventional (unmodified) household microwave oven (LG, Little Cheff, 230 V, ∼50 Hz). Reactions were monitored by thin-layer chromatography (TLC) by comparison with the authentic samples. Melting and boiling points were taken in open capillaries using a paraffin bath, and corrections are applied wherever necessary.[22] Infrared spectra were recorded using KBr pellets for solids and neat for liquids on Nicolet 400D FT-IR spectrophotometer. Yields refer to the isolated yields of the products after purification by silica-gel chromatography.

General Procedure for the Protection of Aldehydes to Acylals

A mixture of aldehyde (1 mmol), acetic anhydride (2 mmol), and *p*-TSA (0.1 mmol, 0.19 g) was stirred at room temperature for the time specified in Table 2. The reaction was followed by TLC (ethyl acetate–light petrol 1:9). After completion of the reaction, the mixture was diluted with Et_2O. The organic layer was washed with aqueous $NaHCO_3$ (5 mL × 2) and water (5 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent under reduced pressure gave almost pure 1,1-diacetate. Further purification by column chromatography gave the corresponding pure product.

General Procedure for the Conversion of Acylals to Aldehydes

A mixture of diacetate (1 mmol), *p*-TSA (0.1 mmol, 0.19 g), and water in CH_3CN (1:1, 1 mL) was irradiated in a commercial microwave oven (320 W) for the time specified in Table 3. The reaction was monitored on TLC (ethyl acetate–light petrol 1:9). At the end of irradiation, the mixture was cooled to room temperature and extracted with diethyl ether. The organic layer was washed with aqueous $NaHCO_3$ (5 mL × 2) and water (5 mL) and dried over anhydrous sodium sulphate. The residue obtained was column chromatographed over silica gel to obtain the pure aldehyde.

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