SHORT PAPER

Efficient and selective protection of aldehydes as geminal diacetates using LiBr[†]
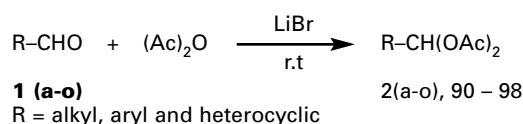
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A variety of aldehydes react with acetic anhydride in presence of lithium bromide at room temperature to afford the corresponding 1,1-diacetates in quantitative yields within a few hours of reaction time.

Aldehydes react with anhydrides in the presence of acid catalysts to form geminal diacetates[1a] (acylals) which are precursors for synthetically important acetoxy dienes[1b] and dihalovinylacetates.[1c] Acylals are also useful as cross linking reagents for cellulose in cotton[1d] and serve as activators in the composition of bleaching mixture used for the treatment of wine-stained fabrics.[1e] Due to remarkable stability of acylals to basic as well as neutral media, they are also gaining importance in organic synthesis as an alternative to acetals for the protection of aldehydes[1f]. A number of methods employed for the preparation of 1,1-diacetates from aldehydes use protic acids such as sulfuric, phosphoric and methane sulfonic acids[2a] or Lewis acids like $ZnCl_2$,[2b] $FeCl_3$,[2c] PCl_3,[2d] *etc.* However, many of these methods suffer from drawbacks such as longer reaction time (up to 120 h in case of 2-furaldehyde with PCl_3), low yields of the product (4% in case of 4-nitrobenzaldehyde[2d]) and other general problems that are associated with any conventional protic or Lewis acid catalysed reactions[2] such as corrosion, effluent and tedious workup procedure *etc.* Attempts have been made to circumvent some of these problems through heterogeneous catalysis involving various types of zeolites[3a] and Nafion-H[3b] resin, including a recent report which uses iodine[3c] as the catalyst.

The potential of lithium halides as the catalysts for various organic transformations is well established[4]. Herein we report a highly efficient and mild method for the quantitative conversion of aldehydes into corresponding diacetates using lithium bromide.

$$R\text{–}CHO \;+\; (Ac)_2O \xrightarrow[\text{r.t}]{\text{LiBr}} R\text{–}CH(OAc)_2$$

1 (a-o)

2(a-o), 90 – 98

R = alkyl, aryl and heterocyclic

Scheme

Thus, diacetates were obtained in excellent yields when different aldehydes were allowed to react with acetic anhydride in the presence of anhydrous lithium bromide. All the reactions were conducted at room temperature under N_2 atmosphere and the reaction progress could be monitored by TLC. The conversion was complete within 2 h in the case of many aldehydes bearing electron donating groups in aromatic ring as well as heterocyclic substrates. However, aromatic aldehydes with electron withdrawing groups and bulky substrates, like anthracene-9-carboxaldehyde and also aliphatic aldehydes, required a comparatively longer reaction time of 3–5 hs to achieve complete conversion. In each case practically pure diacetate was obtained at the end of aqueous work-up, followed by extraction with ethylacetate. This method is very clean and of general applicability as various aliphatic, aromatic, heterocyclic and polynuclear aromatic substrates were readily converted into the corresponding diacetates. Ketones did not react under the above conditions and in the case of substrates bearing both aldehyde and ketone functionalities, the keto group remains unaffected with aldehyde getting converted into 1,1-diacetate which clearly shows the highly selective nature of this reaction.

Table 1   Conversion of aldehydes to geminal diacetates

Product	R[a]	Reaction time (h)	Yield[b] (%)	mp(°C) or bp(°C)/Torr found	reported[2a,c]
2a	Ph	2.0	95	43–45	44–46
2b	$4\text{-}ClC_6H_4$	4.5	94	80–81	79–46
2c	$4\text{-}MeC_6H_4$	1.5	92	77–78	78-80
2d	$4\text{-}NO_2C_6H_4$	5.0	94	123–24	124–25
2e	$4\text{-}CNC_6H_4$	3.5	96	99–100	98–100
2f	Piperonyl	1.5	96	74–75	75–76
2g	Cinnamyl	2.0	90	83–84	84–86
2h	2-Naphthyl	3.0	92	97–98	99–100
2i	2-Furyl	0.5	96	48–49	50–51
2j	2-Thienyl	0.5	98	67–68	66–67
2k	8-Anthracenyl	3.5	92	201–203[5]	—
2l	2-(4–formylphenoxy) 1-phenylethanone	4.0	94	71–73[5]	—
2m	Acetophenone	6.0	No reaction	—	—
2n	C_6H_{13}	4.0	90	127–129/2mm	128–29/2mm
2o	3-Phenylpropanyl	4.0	92	184–88/7mm	185–90/7mm

[a]All products were characterised by IR, ^{1}H NMR, Mass spectroscopic data and also comparison with authentic samples
[b]Isolated yields after work up and recrystallisation (ethylacetate – *n*-hexane, 20:80).

In conclusion, in this paper a simple, highly convenient and general method for the quantitative conversion of the aldehydes into the 1,1-diacetates using inexpensive LiBr is presented. This reaction proceeds smoothly at ambient temperature, strictly under neutral conditions to afford practically pure diacetates within a few hours of reaction.

4-Methyl-1,1-diacetate (2c) : typical procedure

To solution of freshly distilled p-methylbenzaldehyde (**1c**; 1.2 g, 10 mmol) in acetic anhydride (1.42 ml, 15 mmol) was added LiBr (0.865 g, 10 mmol) and stirred at ambient temperature. Progress of the reaction was followed by TLC and after 1.5 h. the reaction mixture was poured into saturated sodium bicarbonate solution (25 ml) and extracted with EtOAc (2 × 20 ml). The combined EtOAc layers were washed with brine (2 × 10 ml), dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Crude product was recrystallised (EtOAc / *n*-hexane) to afford the pure diacetate (**2c**); yield 2.04 g (92%)

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5 **Representative data for compound 2k** : Pale yellow solid, m.p. 201–203°C. ^{1}H NMR ($CDCl_3$) : δ 2.2 (s, 6H), 7.45–7.65 (m, 4H), 8.0 (d, 2H, *J* = 8.5 Hz), 8.5 (s, 1H), 8.70 (d, 2H, *J* = 8.5 Hz), 9.25 (s, 1H). ^{13}C (Proton decoupled, $CDCl_3$) : δ 20.50 (–CH_3), 167.80 (–CO–, 88.56 (–CH<), 125.34, 125.76, 126.35, 127.34, 127.32, 129.85, 130.30, 132.87 (aromatic). Anal. calcd for $C_{19}H_{16}O_4$ (308.33) : C, 74.10; H, 5.33. Found C, 74.25; H, 5.42.
   Compound 2l : Solid, mp 71–73°C. IR υ_{max} / (cm^{-1}) 1680 (–CO–) and 1744 (CH(OAc)2). 1H NMR ($CDCl3$) : d 2.1 (s, 6H), 5.25 (s, 2H), 6.95 (d, 2H, *J* = 8.72 Hz), 7.45-7.55 (m, 5H), 7.6 (s, 1H), 8.0 (d, 2H, *J* = 8.7 Hz). 13C (proton decoupled, $CDCl_3$) : d 20.5 (–CH_3), 167.9 (–CO–), 87.75 (–CH<), 75.95 (–CH_2), 191.33 (–CO-Ph), 114.55, 128.25, 129.29, 130.41, 132.78, 133.36, 188.90 (aromatic). Anal. calcd. for $C_{19}H_{18}O_6$ (342.35) : C, 66.78; H, 5.21. Found C, 66.57; H, 5.38.