1,3-Dibromo-5,5-dimethylhydantoin as catalyst for the conversion of aldehydes to their 1,1-diacetates (acetylals) under solvent-free and neutral conditions

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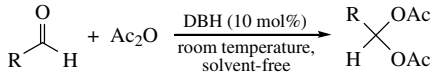
Highly efficient and mild acetylation of aldehydes with acetic anhydride catalysed by 1,3-dibromo-5,5-dimethylhydantoin (DBH) was performed under neutral conditions to produce corresponding 1,1-diacetates (acetylals) in good to excellent yields.

The conversion of aldehydes and ketones to acetals and ketals, respectively, by treatment with alcohols in the presence of acid catalysts has long been used as a useful method of protection of aldehyde or ketone functions from an attack by bases.[1] It is also known that aldehydes can be converted to acylals by treatment with an anhydride in the presence of Lewis acids (*e.g.*, BF_3),[2] proton acids (*e.g.*, H_2SO_4 or Nafion-H)[3] or PCl_3.[4] This reaction cannot normally be applied to ketones, presumably, for steric reasons, except when the reagent is trichloroacetic anhydride, which gives acylals with ketones without a catalyst.[5] More recently, zeolites[6] and iodine[7] have also been reported as efficient catalysts employed in these reactions. Ishihara and his co-workers have used scandium triflates [*e.g.*, $Sc(OTf)_3$ and $Sc(NTf_2)_3$] to catalyse the acylation of carbonyl compounds.[8]

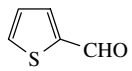
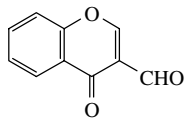
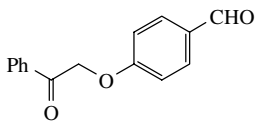
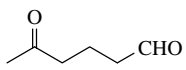


1a–m **2a–m**

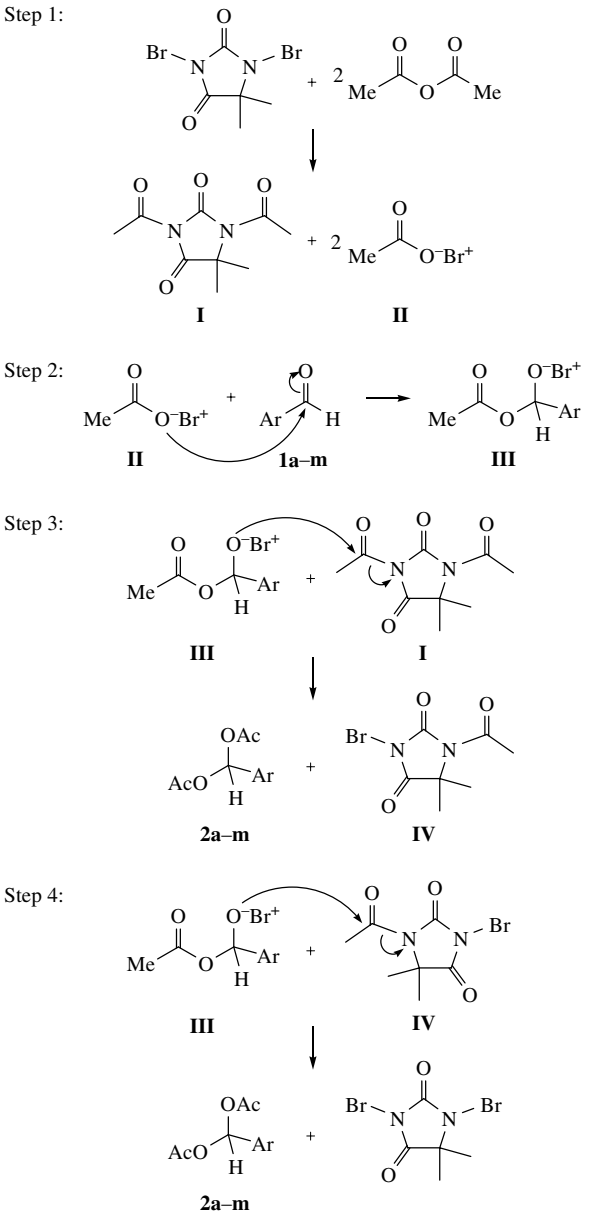
Scheme 1

To avoid the strong acids used in the previously reported protocols and long reaction times, here, we report on the catalytic activity of 1,3-dibromo-5,5-dimethylhydantoin (DBH) in the reaction of aldehydes **1a–m** with acetic anhydride under solvent-free and neutral conditions to afford corresponding acetylals **2a–m** in good to excellent yields (87–99%) (Scheme 1, Table 1).†

Table 1 DBH-catalysed conversion of aldehydes **1a–m** to 1,1-diacetals (acetylals) **2a–m** with Ac_2O under solvent-free conditions.

Substrate	RCHO	Time/h	Product[a] [yield (%)[b]]	Mp/°C
1a	PhCHO	1.5	**2a** (98)	43–45
1b	4-$NO_2C_6H_4CHO$	2.0	**2b** (92)	116–118
1c	4-ClC_6H_4CHO	0.7	**2c** (99)	76–78
1d	2-ClC_6H_4CHO	1.0	**2d** (98)	70–72
1e	3-$NO_2C_6H_4CHO$	2.2	**2e** (98)	110–112
1f	4-MeC_6H_4CHO	0.9	**2f** (99)	79–81
1g	2-MeC_6H_4CHO	1.2	**2g** (98)	75–77
1h	2-$MeOC_6H_4CHO$	1.0	**2h** (95)	58–60
1i	PhCH=CHCHO	0.8	**2i** (92)	78–80
1j		2.5	**2j** (90)	65–67
1k		3.0	**2k** (95)	85–87
1l		1.2	**2l** (87)	158–160
1m		2.8	**2m** (98)	–35

[a]All products were characterised by IR and ^{1}H NMR spectroscopy and mass spectrometry. [b]Isolated yields.



Scheme 2

We also investigated the chemoselective conversion of aldehydes to acetylals in the presence of ketones such as benzophenone, acetophenone and cyclohexanone. It was shown that, when a 1:1 mixture of benzaldehyde and acetophenone was allowed to react with acetic anhydride (10 mmol) in the presence of DBH (10 mol%), and the reaction mixture worked up after 2 h, the crude products consisted of a 1:1 mixture of benzaldehyde acetylal and unreacted acetophenone as indicated

by NMR analysis. This provides chemoselective conversion of an aldehyde to acetylal without affecting the ketone functionality. In addition, the chemoselectivity of the method was observed by the use of keto aldehydes **1k**–**m**, which reacted merely at the aldehyde group to produce corresponding 1,1-diacetates in high yields without the ketone functionality being affected. This suggests that DBH can be selectively used to convert the aldehyde groups into their acetylal form in the presence of ketone functionalities. A possible mechanism suggested for this reaction is shown in Scheme 2. In step 1, the N,N-diacetylation of DBH occurs to afford 1,3-diacetyl-5,5-dimethylhydantoin **I** and bromium acetate **II**, which undergoes a nucleophilic addition to the aldehyde in step 2 to yield an anionic acetyloxy adduct **III**. The nucleophilic substitution of both N-acetyl groups of **I** by adduct **III** in two successive steps 3 and 4 results in the production of acetylal compounds **2a**–**m** and regeneration of the DBH catalyst.

† Chemicals were obtained from Merck and Fluka. IR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets), and NMR spectra were measured in $CDCl_3$ using a 90 MHz Jeol FT NMR spectrometer. All melting points were determined on a Büchi 530 melting point apparatus and reported uncorrected.

Conversion of aldehydes **1a**–**m** *to acetylals* **2a**–**m** *with* Ac_2O *catalysed by DBH. General procedure*. To a magnetically stirred solution of aldehyde **1a**–**m** (5 mmol) and freshly distilled acetic anhydride (1.02 g, 10 mmol), DBH (0.143 g, 0.5 mmol) was added at room temperature and the resulting mixture was stirred for 1–3 h. After the complete disappearance of starting materials, as monitored by TLC using EtOAc/petroleum ether (1:9) or by ^{1}H NMR analysis, the mixture was extracted with diethyl ether (2×20 ml). The organic layer was then separated, washed with distilled water (15 ml) and dried over anhydrous Na_2SO_4. Evaporation of the solvent under reduced pressure resulted in highly pure products **2a**–**m** in 87–99% yields (Table 1) and no further purification was necessary. The structures of the products were established on the basis of their ^{1}H NMR, ^{13}C NMR and mass spectra and by a direct comparison with the authentic compounds.[7,9]

In conclusion, we found that the use of Ac_2O/DBH offers a simple and convenient method for the conversion of aliphatic and aromatic aldehydes to their acetylals in excellent yields (87–99%). The neutrality of the reaction media that avoids strong acids, high selectivity of the reaction between aldehyde and ketone carbonyl groups, easy work-up procedure, high yields, mildness of the reactions and solvent-free conditions make this method suitable for the direct conversion of aldehydes into acetylals.

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