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A facile chemoselective deacetylation in the presence of benzoyl and *p*-bromobenzoyl groups using *p*-toluenesulfonic acid

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Abstract—The acetyl group was chemoselectively cleaved in the presence of *p*-toluenesulfonic acid (*p*-TsOH) in CH_2Cl_2/MeOH without affecting the benzoyl (benzoate and *p*-bromobenzoate) groups and no transesterification product was observed. The treatment of protected carbohydrates with *p*-TsOH·H_2O at room temperature usually required a longer reaction time than at 40°C. Other types of sulfonic acid such as 10-camphorsulfonic (CSA) led to similar results. © 2001 Elsevier Science Ltd. All rights reserved.

The acetyl group is a very useful protecting group and it has been employed widely in the synthesis of natural products and in carbohydrate chemistry.[1] The acetate is the protecting group in ester form, it is easy to introduce, and several methods exist to cleave it.[1]

It is known that different esters used as protecting groups can be deprotected selectively, such as formate that can be deprotected in the presence of acetate and benzoates;[2,3] trichloroacetate in the presence of acetate and formate;[4] trichloroethylcarbonate that can be deprotected selectively using zinc,[5] etc.

Several reagents have been reported that allow *O*-deacetylation in the presence of benzoates, e.g. guanidine,[6] guanidine/guanidinium,[7] Sm/I_2,[8] DBU,[9] etc. Several reactions were developed under acid conditions using HCl/MeOH[10–12] and HBF_4·Et_2O in MeOH,[13] respectively. This last reagent was found to be superior to HCl/MeOH which had been the standard reagent in the removal of the *O*-acetyl group in the presence of *O*-benzoyl groups.[14] We present herein a method for acetate cleavage that can be accomplished in the presence of other esters such as benzoates and *p*-bromobenzoates and promoted by *p*-toluenesulfonic acid (*p*-TsOH), which has been used before in the deacetylation of aryl acetates.[15] The reaction was quite clean, no transesterification product was observed and the yields were uniformly reproducible.

The results of the cleavage of the acetate group in various substrates under our conditions are summarized in Table 1. Two acetates were removed chemoselectively in the presence of two benzoyl groups at 40°C in 7 h (entry 1) with excellent yield. At room temperature the reaction took 24 h with similar yields. Using another sulfonic acid such as 10-camphorsulfonic acid (CSA) we obtained good yields but the reaction time was much longer than with *p*-TsOH: 3 days at rt and 2 days at 40°C. In the case of a primary benzoate (entry 2) the best result was achieved at room temperature since at 40°C this benzoate was also removed. However, we solved this problem by using *p*-bromobenzoate instead of benzoate (entry 4), because the former is more stable. We can take advantage of this reaction in carbohydrate chemistry (entry 6), deacetylating a unit of monosaccharide against another unit fully protected as *p*-bromobenzoate.

A typical procedure used in the above deprotection reactions follows: The substrate was dissolved in CH_2Cl_2/MeOH (9:1) and then *p*-TsOH·H_2O (1.0 equiv. per acetate) was added. The resulting mixture was stirred at room temperature or at 40°C and the reaction was monitored by TLC. After the reaction was completed, the mixture was extracted with CH_2Cl_2 and the organic phase washed with aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The product was purified by flash column chromatography.

In conclusion, we have developed a highly efficient chemoselective reaction for deacetylation in carbohydrates. In general, cleavage of acetates can be accom-

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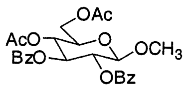
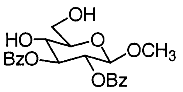
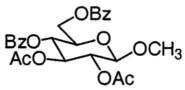
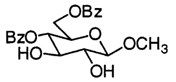
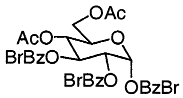
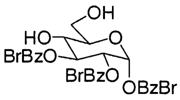
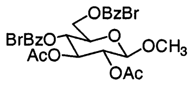
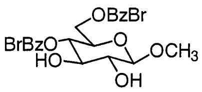
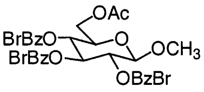
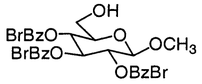
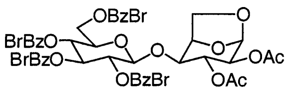
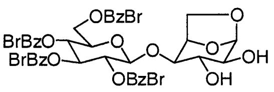
Table 1. *O*-Deacetylation in the presence of benzoates and *p*-bromobenzoates

Entry	Substrates	Conditions	Products[a]	Yield[b]
1		***p*-TsOH (2 equiv)** **40° C, 7 h** **CSA (2 equiv)** **rt, 72 h**		91 % 88 %
2		***p*-TsOH (2 equiv)** **rt, 24 h**		65 %
3		***p*-TsOH (2 equiv)** **rt, 24 h**		90 %
4		***p*-TsOH (2 equiv)** **40° C, 24 h**		70 %
5		***p*-TsOH (1 equiv)** **40° C, 24 h**		88 %
6		***p*-TsOH (2 equiv)** **40° C, 24 h**		70 %

[a]. All products were characterized by ^{1}H NMR and ^{13}C NMR.
[b]. Isolated yields.

plished in the presence of other esters such as benzoates and *p*-bromobenzoates. We propose the use of acetate/*p*-bromobenzoate as a tandem of protecting groups in carbohydrate chemistry (entry 6).

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