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A New Convenient Method for Selective Monobenzoylation of Diols

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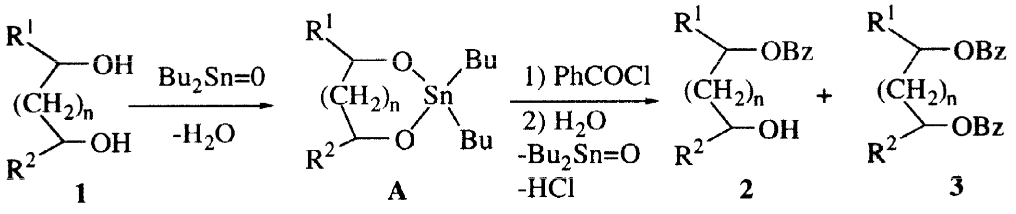
Abstract

A new facile method for monoacylation of diols has been developed. A variety of cyclic and acyclic diols, in particular 1,2-diols, was selectively monobenzoylated in good yields by their reaction with benzoyl chloride in the presence of a catalytic amount of dimethyltin dichloride and inorganic bases.

keywords: Tin and compounds; Diols; Acylation

Selective protection of a hydroxyl group of polyols is very important in organic synthesis [1-4]. Dibutyltin oxide has been known to be a useful reagent for monobenzoylation of diols **1** since it preferentially reacts with **1** to form dibutylstannylene acetals **A** which are used for the subsequent benzoylation reaction (eq 1) [5-9]. The method, however, possesses some drawbacks. Namely, **A** must be prepared by heating with a long reaction time in advance to the benzoylation because of the slow dehydration reaction between **1** and dibutyltin oxide. This imposes the use of more than an equimolar amount of dibutyltin oxide which will complicate the purification process of the products and make the large-scale production of monobenzoylated products **2** difficult. Recently, a microwave irradiation method has been reported to reduce the amount of dibutyltin oxide. However, this method still possesses disadvantages that a microwave apparatus is required and the irradiation conditions might be drastic [10-12]. Moreover, dibenzoates **3** are often formed as by-products in the benzoylation of **1** using dibutyltin oxide.



(1)

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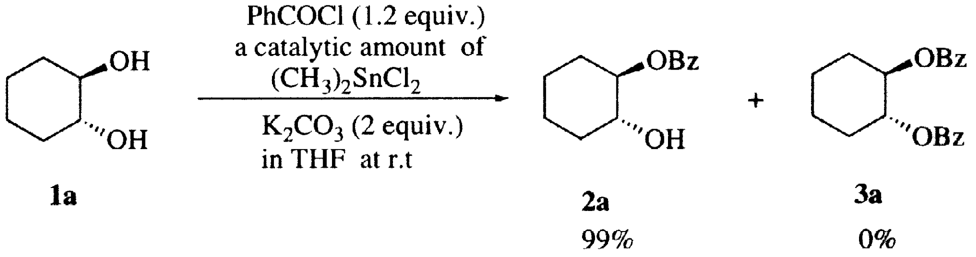
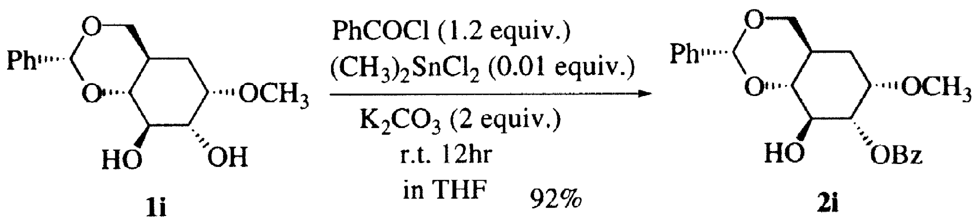
We report herein a very convenient method for the monobenzoylation of **1** which is achievable in a one-pot procedure with less than 0.01 equivalent amount of tin catalysts under mild conditions. Our method is also characterized by the high yields of **2** and an excellent 1,2-diol-selectivity with a minimized formation of **3**.

A key point in our method is the use of both dimethyltin dichloride[1] instead of dibutyltin oxide and inorganic bases[2] like K_2CO_3 in organic solvents[3] such as tetrahydrofuran. A typical reaction is exemplified by the benzoylation of *trans*-1,2-cyclohexanediol **1a** to give the monobenzoylated product **2a** in 99% yield without any formation of the dibenzoate **3a** (eq 2). The reaction procedures were very simple and easy. That is, to a tetrahydrofuran (5 mL) solution of **1a** (1 mmol) were added a catalytic amount of dimethyltin dichloride (0.01 mmol), solid K_2CO_3 (2.0 mmol) and benzoyl chloride (1.2 mmol), successively, at room temperature. After stirring the mixture at room temperature until **1a** disappeared (checked by thin layer chromatography), the mixture was poured onto water and the organic portion was extracted with CH_2Cl_2. After evaporation of the solvent, a residue was obtained and confirmed by NMR to be pure **2a** (>99%).



(2)

Our method is applicable to other 1,2- and 1,n-diols such as **1b-h** under similar reaction conditions. The results are summarized in Table 1. As shown in Table 1, monobenzoylation of 1,2-diols **1a-d** took place quantitatively (runs 1-4). On the other hand, diols **1e-h** other than 1,2-diols were slowly monobenzoylated in moderate yields (runs 5 and 7). Those yields were improved by using larger amount (0.1 equiv.) of dimethyltin dichloride (runs 6, 8-10). Benzoylation of unsymmetrical 1,2-diol **1i** took place only at the 2-hydroxyl group (eq 3), while that of **1j** preferentially occurred at the less substituted site to give **2j** in good yield with a small amount of **2j'** (eq 4).



(3)

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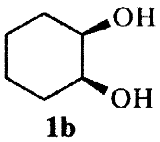
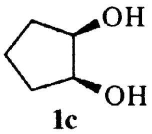
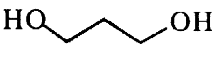
[1] Dibutyltin dichloride was usable, though the yields of monobenzoates were lower (78%) than those in cases using dimethyltin dichloride.

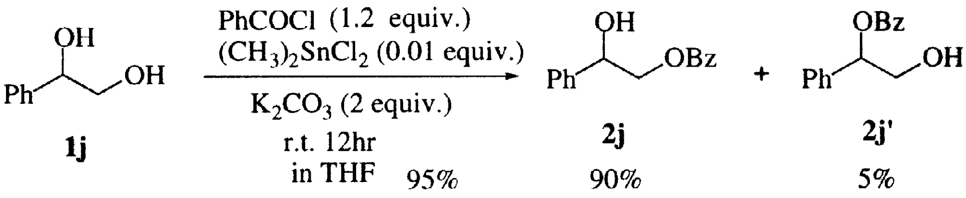
[2] Commercially available sodium carbonate gave relatively lower yields (~ 90%) of monobenzoylated product.

[3] Methylene chloride was usable instead of tetrahydrofuran.

Table 1. Monobenzoylation of Diols **1a-h** catalyzed by Dimethyltin Dichloride[a]

Run	Diol **1**	$(CH_3)_2SnCl_2$ Equivalent to **1**	Reaction time hr	Yield(%)[b] of **2**		**3**	
1	**1a**	0.01	5	**2a**	99	**3a**	0
2	 **1b**	0.01	12	**2b**	99	**3b**	0
3	 **1c**	0.01	12	**2c**	~100	**3c**	0
4	 **1d**	0.01	12	**2d**	~100	**3d**	0
5	 **1e**	0.01	12	**2e**	67[c]	**3e**	trace
6	**1e**	0.1	12	**2e**	80[c]	**3e**	4.6
7	 **1f**	0.01	12	**2f**	51[c]	**3f**	0
8	**1f**	0.1	12	**2f**	65[c]	**3f**	0
9	$HO(CH_2)_5OH$ **1g**	0.1	12	**2g**	46[c]	**3g**	5.7
10	$HO(CH_2)_6OH$ **1h**	0.1	12	**2h**	48[c]	**3h**	4.2

a) The amount of benzoyl chloride used was 1.2 equivalent to diols. b) Isolated yield.
c) The starting diol remained.

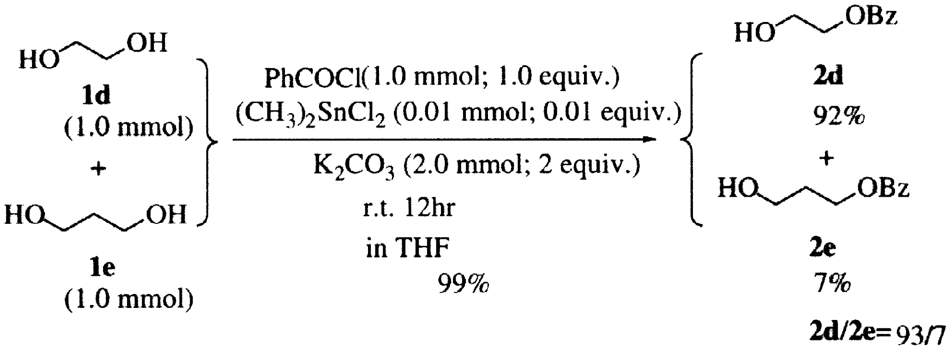


(4)

The advantage of our method is its high diol selectivity. For example, **1a** was selectively benzoylated even in the presence of 5 molar equivalent of *n*-butanol to give **2a** in 89% yield without the formation of *n*-butyl benzoate (eq 5). Thus, *n*-butanol was inert under these reaction conditions.

$$\mathbf{1a} + \underset{\text{(5 equiv.)}}{n\text{-BuOH}} \xrightarrow[\substack{K_2CO_3\ (2\ \text{equiv.}) \\ \text{r.t. 5hr} \\ \text{in THF}}]{\substack{PhCOCl\ (1.2\ \text{equiv.}) \\ (CH_3)_2SnCl_2\ (0.01\ \text{equiv.})}} \underset{89\%}{\mathbf{2a}} \qquad (5)$$

The selectivity in our method was also exemplified by a competitive reaction between 1,2-diol and 1,3-diol.[4] That is, the addition of benzoyl chloride to an equimolar amount of **1d** and **1e** in the presence of K_2CO_3 and a catalytic amount of dimethyltin dichloride exclusively gave benzoylated product **2d** in 92% yield with a small amount of **2e** (7% yield) (eq 6), suggesting that the benzoylation is highly selective to 1,2-diols. These selectivities should be very useful for the synthetic utilization of this method.



(6)

Although the reasons behind those reactivities and selectivities are not clear yet, undoubtedly the proposed method is not only very convenient for monoacylation of diols but also worthwhile from the viewpoint of environmental pollution since the catalytic amount of dimethyltin dichloride is enough to complete the monobenzoylation[5] and the reaction can be achieved by very simple procedures under mild conditions. Further studies on the mechanistic aspects and asymmetric application are now under investigation.

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(4) The benzoylation of a mixture of an equimolar amount of 1,2-diols **1a** and **1d** afforded **2a** and **2d** in 44% and 55% yields, respectively.

(5) The catalytic cycle of tin reagent can be explained in terms of the benzoylation of dimethylstannylene acetals similar to **A** followed by the reaction of the resulting benzoylated alkoxytin intermediates with **1** to regenerate the acetals.