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A novel 3-nitrobenzeneboronic acid as an extremely mild and environmentally benign catalyst for the acetylation of alcohols under solvent-free conditions

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Abstract—A novel 3-nitrobenzeneboronic acid is found to catalyse efficiently the acetylation of a wide range of alcohols as well as phenols with acetic anhydride in good to excellent yields at room temperature under solvent-free conditions. The reactions are clean and the catalyst is mild such that highly sensitive functional groups including oximes are stable to the reaction conditions.

With increasing environmental concerns and the regulatory constraints faced in the chemical and pharmaceutical industries, the development of environmentally benign organic reactions has become a crucial and demanding area in modern organic chemical research.[1] According to Wender, the 'ideal synthesis' is one in which the target components are readily obtained in one step and in quantitative yields from readily available starting materials in an environmentally acceptable process.[2] Acetylation of alcohols is an important and common transformation in organic synthesis.[3] In general, acetyl chloride or acetic anhydride, in the presence of a tertiary amine such as triethylamine or pyridine, is used for the acetylation of alcohols.[4] For practical reasons, the latter is usually preferred. The use of 4-(dimethylamino)pyridine (DMAP)[5] as a co-catalyst accelerates the acetylation process. However, to overcome the problems associated with these basic catalysts, the use of Bu_3P for acetylation of base sensitive alcohols was reported by Vedjes et al.[6] In addition, protic and Lewis acids, and on some occasions, solid acids have also been reported to be effective for catalysing the acetylation of alcohols.[7]

In view of the synthetic importance of this reaction, a plethora of catalysts for acetylation have been introduced including simple metal salts such as $COCl_2$,[8] $ZnCl_2$,[9] $TiCl_4$–$AgClO_4$,[10] Me_3SiCl,[11] $LiClO_4$[12] and $MgClO_4$[13] as well as metal triflates such as $Sc(OTf)_3$,[14] Me_3SiOTf,[15] $In(OTf)_3$,[16] $Cu(OTf)_3$[17] and $Bi(OTf)_3$.[18] Recently, perchlorates were reported to catalyse the acetylation of alcohols, however, perchlorates, particularly of lithium, are reported to be explosive and moisture sensitive. Very recently, molecular iodine catalysed acetylation of alcohols was reported.[19]

Although a large number of methods for acetylation are available, the practical applicability of most of these methods suffers from limitations such as the use of, (1) expensive, moisture sensitive and toxic catalysts, (2) long reaction times and (3) a lack of generality. In view of the modern demands of organic synthesis,[1] there is still the need to develop an efficient, mild and environmentally benign protocol for the acetylation of alcohols.

In recent years, we have been engaged in evaluating the catalytic potential of arylboronic acids, particularly those with electron withdrawing substituents, in organic synthesis.[20] We reported that 3-nitrobenzeneboronic acid **1** efficiently catalysed the selective transesterification of β-ketoesters under mild conditions.[21] We reasoned that, catalyst **1**, might also activate anhydrides for acetylation of alcohols. Herein, we report that various alcohols can be acetylated with acetic anhydride efficiently, in good to excellent yields, in the presence of **1** (2.5 mol %) at room temperature under solvent-free conditions (Scheme 1).

Keywords: 3-Nitrobenzeneboronic acid; Solvent-free reaction; Acetylation; Deoximation.
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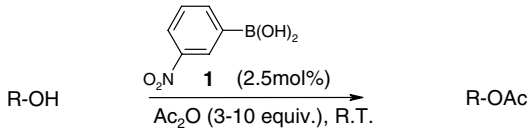


Scheme 1.

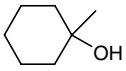
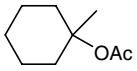
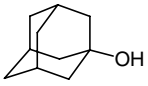
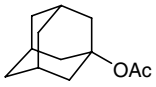
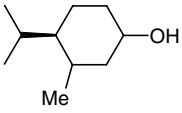
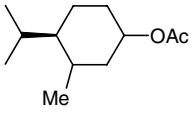
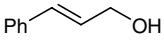
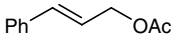
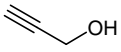
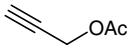
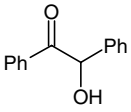
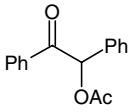
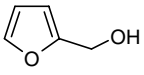
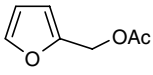
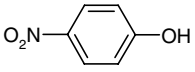
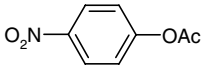
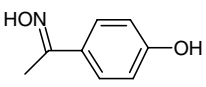
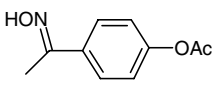
Table 1. Acetylation of *n*-decanol with acetic anhydride catalysed by **1**[a]

Entry	Catalyst (mol %)	Time (h)	Yield[b] (%)
1	1.0	10	42
2	1.5	10	56
3	2.0	10	78
4	2.5	10	90
5	2.5	7	95[c]

[a] All the products gave satisfactory spectral data (IR, ^{1}H NMR).
[b] Isolated yield.
[c] 0.2 equiv of $MgSO_4$ was added.

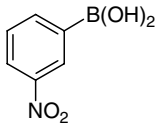
In order to establish the best reaction conditions, we performed an optimisation study using *n*-decanol as the model substrate in the presence of varying amounts of catalyst **1**, might also activate anhydrides for acetylation of alcohols. As shown in Table 1, 2.5 mol % of catalyst was found to be effective for acetylation of *n*-decanol in 95% yield within 7 h. A threefold excess of acetic anhydride was effective for the reaction to proceed at a reasonable rate. To explore the generality and scope of the method, other alcohols and phenols were acetylated with acetic anhydride using our optimised reaction conditions. The results are collected in Table 2. Structurally diverse alcohols such as primary, secondary, allylic and propargylic alcohols underwent smooth acetylation in good to excellent yields and, in some cases, in quantitative yields. Notably, hindered tertiary alcohols such as 1-methylcyclohexanol and adamantanol (entries 5 and 6) were acetylated cleanly and efficiently under the present reaction conditions in high

Table 2. Acetylation of alcohols and phenols catalysed by 3-nitrobenzeneboronic acid **1**[a]

Entry	Substrate	Product	Time (h)	Yield[b] (%)
1	*n*-$C_{10}H_{21}OH$	*n*-$C_{10}H_{21}OAc$	7	95
2	*n*-$C_8H_{17}OH$	*n*-$C_8H_{17}OAc$	6	90
3	Benzyl alcohol	Benzyl acetate	10	90
4	4-Nitrobenzyl alcohol	4-Nitrobenzyl acetate	12	94
5			14	86
6			16	89
7			14	97
8			11	95
9			14	91
10	Ph_2CHOH	Ph_2CHOAc_2	12	>99[c]
11			17	>99[c]
12	Cholesterol	Cholesterol acetate	15	>99[d]
13			10	92
14			8	90
15			12	95[d]

[a] All the reactions were performed using 3 equiv of acetic anhydride unless otherwise stated.
[b] Isolated yields.
[c] To solubilise solid alcohol, 5 equiv of acetic anhydride was added.
[d] The reactions were performed using 10 equiv of acetic anhydride.

Table 3. Selective acetylation of 4-hydroxyacetophenone oxime using various catalysts[a]

Entry	Catalyst	Time (h)	Selectivity[b] (%)
1		12	95
2	$In(OTf)_3$[c]	0.1	0
3	$LiClO_4$	22	82

[a] All reactions were performed using 5 equiv of acetic anhydride in the presence of 2.5 mol % of the catalyst at room temperature.
[b] Isolated yield of 4-acetyloxyacetophenone oxime.
[c] 4-Acetyloxyacetophenone was obtained as the only product within 5 min.

yields. Moreover, acid sensitive alcohols such as furfuryl alcohol (entry 13) were acetylated in excellent yields without giving any side products. The reaction can also be applied to the acetylation of phenols. The extremely mild behaviour of catalyst **1** was evident from the fact that the acetylation of 4-hydroxyacetophenone oxime (entry 15) was achieved in high yield with no deprotection observed at all.

To expand the scope of the present reaction further, we performed a comparative study in which the selective acetylation of 4-hydroxyacetophenone oxime using our catalyst was compared with $In(OTf)_3$ and $LiClO_4$ under solvent-free conditions. The results are collected in Table 3. Indium triflate catalysed the acetylation (Table 3, entry 2) extremely fast and the reaction was complete within 5 min, but only with concomitant deprotection of the oxime to give the corresponding 4-acetyloxyacetophenone as the only product. However, acetylation using $LiClO_4$ (Table 3, entry 3) gave comparable selectivity, however, the reaction took longer to reach completion. Although the rate of acetylation with **1** is less than those catalysed by expensive metal triflates, it is faster than those involving catalysts (10–20 mol %) such as $LiClO_4$, and NBS, and gives comparable yields of products despite using only 2.5 mol % of the catalyst. Unfortunately, all attempts to acetylate diols by this method proved fruitless. The probable reason for this failure is that the catalyst might be trapped by the diol as boronic acids react readily with diols to form 1,3,2-dioxaborolanes.

Arylboronic acids are usually crystalline solids, stable to air and moisture. Such evidence as exists, indicates that they are of relatively low toxicity [benzeneboronic acid, LD_{50}, oral rat = 740 mg/kg] and have low environmental impact. Moreover, a small amount of boronic acid **1** (2.5 mol %) is effective as a catalyst for the acetylation of alcohols and phenols.

General procedure for the acetylation of alcohols and phenols:
A mixture of the alcohol or phenol (2 mmol), acetic anhydride (3–10 mmol) and catalyst **1** (0.025 mmol) was stirred at room temperature for the time indicated in Table 2. After completion, the reaction was quenched with water (20 cm^3). The mixture was extracted with ethyl acetate (2×30 cm^3) and the combined organic layer was washed with saturated $NaHCO_3$ (2×20 cm^3) and brine (20 cm^3). Evaporation of the solvent followed by purification by column chromatography (silica gel, eluent, ethyl acetate–hexane 1:9) gave the pure acetate.

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References and notes

1. Anastas, P.; Williamson, T. *Green Chemistry, Frontiers in Benign Chemical Synthesis and Procedures*; Oxford Science Publications: Oxford, 1998.
2. Wender, P. A.; Handy, S. L.; Wright, D. L. *Chem. Ind. (London)* **1997**, 765.
3. Green, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; John Wiley and Sons: New York, 1999, p 150.
4. Larock, R. C. *Comprehensive Organic Transformations*; VCH: New York, 1989, p 980.
5. Steglich, W.; Hofle, G. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 981.
6. Vedjes, E.; Bennett, N. S.; Conn, L. M.; Diver, S. T.; Gingras, M.; Lin, S.; Oliver, P. A.; Peterson, M. J. *J. Org. Chem.* **1993**, *58*, 7286.
7. Iqbal, J.; Srivastava, R. R. *J. Org. Chem.* **1992**, *57*, 2001.
8. (a) Backer, R. H.; Bordwell, F. G. *Org. Synth.* **1955**, *3*, 141; (b) Miyashita, M.; Shiina, I.; Miyoshi, S.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1516.
9. Kumareswaran, R.; Gupta, A.; Vankar, Y. D. *Synth. Commun.* **1997**, *27*, 277.
10. Nakae, Y.; Kusaki, I.; Sato, T. *Synlett* **2001**, 1584.
11. Bartoli, G.; Bosco, M.; Dalpozzo, R.; Marcantoni, E.; Massaccesi, M.; Rinaldi, S.; Sambri, L. *Synlett* **2003**, *39*.
12. Ono, F.; Negoro, R.; Sato, T. *Synlett* **2001**.
13. Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H. *J. Org. Chem.* **1996**, *61*, 4560.
14. Procopiou, P. A.; Baugh, S. P. D.; Flack, S. S.; Inglis, G. G. A. *J. Org. Chem.* **1998**, *63*, 2342.
15. Chauhan, K. K.; Frost, C. G.; Love, I.; Waite, D. *Synlett* **1999**, 1743.
16. Chandra, K. L.; Saravanan, P.; Singh, R. K.; Singh, V. K. *Tetrahedron* **2002**, *58*, 1369.
17. (a) Orita, A.; Tanahashi, C.; Kakuda, A.; Otera, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2877; (b) Orita, A.; Tanahashi, C.; Kakuda, A.; Otera, J. *J. Org. Chem.* **2001**, *66*, 8926.
18. (a) Schumacher, J. C. Perchlorates—Their Properties, Manufacture and Use. In *ACS Monograph Series*; Reinhold: New York, 1996; (b) Long, J. *Chem. Health Saf.* **2002**, *9*, 12.
19. Phukan, P. *Tetrahedron Lett.* **2004**, *45*, 4785.
20. (a) Tale, R. H.; Patil, K. M. *Tetrahedron Lett.* **2002**, *43*, 9715; (b) Tale, R. H.; Patil, K. M.; Dapurkar, S. E. *Tetrahedron Lett.* **2003**, *44*, 3427; (c) Sagar, A. D.; Tale, R. H.; Adude, R. N. *Tetrahedron Lett.* **2003**, *44*, 7140.
21. Tale, R. H.; Sagar, A. D.; Adude, R. N.; Santan, H. D. *Synlett* **2006**, 417.