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Tris(pentafluorophenyl)borane: a mild and efficient catalyst for the chemoselective tritylation of alcohols

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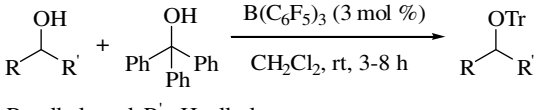
Abstract

An efficient acid-catalyzed protection of alcohols as trityl ethers is described using triphenylmethanol in the presence of tris(pentafluorophenyl)borane (3 mol %) in dichloromethane at room temperature. The chemoselectivity of this protocol is demonstrated by studying the tritylation of a primary alcohol in the presence of a secondary alcohol and also the mildness of this catalyst was studied with substrates containing acid labile protecting groups.

Keywords: Tris(pentafluorophenyl)borane; Chemoselective; Tritylation; Alcohol; Lewis acid

The development of efficient and practically useful Lewis acid catalysts for various organic transformations is of great importance. Tris(pentafluorophenyl)borane [$B(C_6F_5)_3$] is one such Lewis acid catalyst, which is being pursued as a mild and environmentally benign catalyst for various acid catalyzed transformations.[1–10] It is a non-conventional, air-stable, water-tolerant, and thermally stable Lewis acid. Recently, our research group was engaged in exploring the potential utility of $B(C_6F_5)_3$ for various organic transformations such as ring-opening of epoxides, and aza-Ferrier glycosylation,[11–13] and also as an efficient activator for polymethylhydrosiloxane in the reduction of different functional groups.[14,15] In continuation, we report the application of $B(C_6F_5)_3$ in the chemoselective protection of alcohols as trityl ethers in a mild acidic medium.

The triphenylmethyl (trityl) group is a commonly used protecting group for primary alcohols especially in carbohydrate and nucleoside chemistry.[16–18] The introduction of this group to a hydroxyl functionality is traditionally carried out with trityl chloride in the presence of a base.[19–21] Several other reagents such as AgOTf–TrCl,[22] TrODT–TrATCl$_5$,[23] tritylated pyridones,[24] BnOTr–DDQ,[25] TrOTMS–TMSOTf,[26] and *p*-methoxybenzyl trityl ether (*p*-MBTE) or prenyl trityl ether (PTE)–DDQ[27] are also available. Most of these tritylating reagents are not available commercially and have to be prepared from trityl chloride. To date, there are very limited examples known in the literature describing the protection of alcohols as trityl ethers with triphenylmethanol (as tritylating agent) in the presence of an acid catalyst.[28–31] The reaction conditions employed in some of these methods involve strong acidic conditions (H_2SO_4, $FeCl_3$, etc.). Furthermore, these catalysts were studied using only a few examples and no systematic study on chemoselectivity has been carried out. Thus, the development of a new Lewis acid for chemoselective protection of alcohols as trityl ethers under mild reaction conditions is interesting. Here we disclose our findings wherein $B(C_6F_5)_3$ has been identified as a mild and chemoselective Lewis acid catalyst for the said transformation (Scheme 1).



R= alkyl, aryl; R'= H, alkyl

Scheme 1. $B(C_6F_5)_3$-catalyzed tritylation of alcohols.

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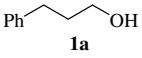
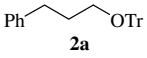
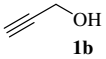
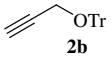
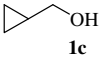
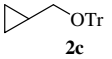
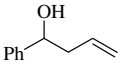
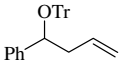
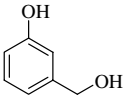
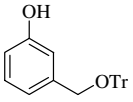
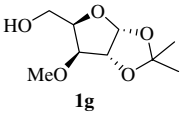
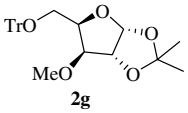
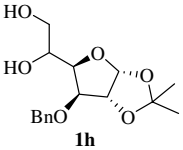
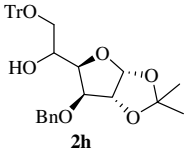
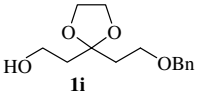
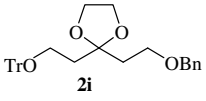
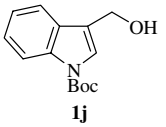
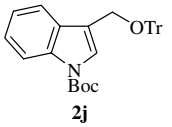
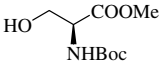
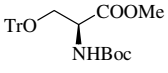
Initially, 3-phenyl-1-propanol **1a** was treated with triphenylmethanol in the presence of 3 mol % $B(C_6F_5)_3$ in dichloromethane at room temperature. The reaction proceeded smoothly in 3 h and afforded the corresponding trityl ether **2a** in 92% isolated yield (Table 1, entry 1). The scope of the reaction conditions was then tested for protection of various other alcohols and the results are summarized in Table 1. The primary alcohols **1b** and **1c** reacted well to yield the trityl ethers **2b** and **2c** in 87 and 93% yields, respectively (Table 1, entries 2 and 3). The secondary benzyl alcohols **1d** and **1e** reacted slowly at room temperature, however, they reacted under refluxing conditions to provide the corresponding trityl ethers **2d** and **2e** in 48 and 56% yields, respectively (Table 1, entries 4 and 5). Entry 6 (Table 1) demonstrates the chemoselective protection of a primary benzylic alcohol in the presence of a phenolic hydroxyl group. Substrates **1g** to **1i** were selectively converted to the trityl ethers **2g** to **2i**, without effecting the acid-labile acetonide, ketal, and benzyl protecting groups (Table 1, entries 7–9). Similarly, the reaction succeeded with alcohols **1j** and **1k**, keeping the acid-sensitive *tert*-butylcarbamate (NBoc) protecting group intact (Table 1, entries 10 and 11).

To check the compatibility and to confirm the mildness of the reagent system, we studied the protection of 1,3-propanediol monoether substrates **3a** to **3h** having a free-hydroxyl group at one end and a hydroxyl-protecting group at the other end. These substrates underwent tritylation at the free hydroxyl group without affecting the other protecting groups (Table 2, entries 1–8).

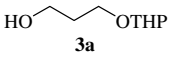
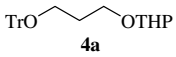
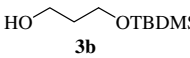
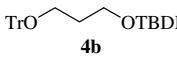
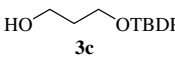
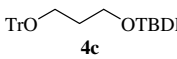
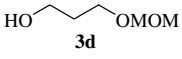
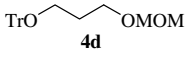
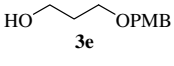
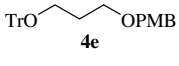
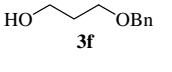
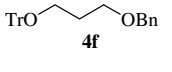
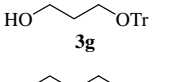
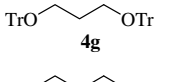
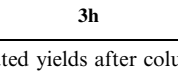
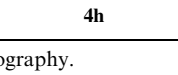
The efficiency of other Lewis acids was also investigated for this transformation using 3-phenylpropanol as a model substrate (Table 3). Treatment of 3-phenylpropanol with triphenylmethanol in the presence of 3 mol % of $BF_3{\cdot}Et_2O$ led to a complex mixture (Table 3, entry 1). The other acid catalysts, $ZnCl_2$, $AlCl_3$, *p*-TSA, and I_2 catalyzed the tritylation (Table 3, entries 2–5). Among these catalysts, $B(C_6F_5)_3$ was found to be more effective in terms of yield, reaction profile, and selectivity (Table 3, entry 6).

Table 1
$B(C_6F_5)_3$-catalyzed tritylation of alcohols

Entry	Substrate	Time (h)	Product	Yield[a] (%)
1	 **1a**	3	 **2a**	92
2	 **1b**	3.5	 **2b**	87
3	 **1c**	4	 **2c**	93
4	 **1d**	8	 **2d**	48[b]
5	 **1e**	8	 **2e**	56[b]
6	 **1f**	4.5	 **2f**	88
7	 **1g**	4	 **2g**	90
8	 **1h**	3.5	 **2h**	90
9	 **1i**	4	 **2i**	94
10	 **1j**	4	 **2j**	87
11	 **1k**	3.5	 **2k**	95

[a] Isolated yields after column chromatography.
[b] Yield from the reaction carried out at reflux.

Table 2
Tritylation of alcohols in the presence of other protecting groups

Entry	Substrate	Time (h)	Product	Yield[a] (%)
1	 **3a**	3	 **4a**	90
2	 **3b**	3.5	 **4b**	92
3	 **3c**	4	 **4c**	94
4	 **3d**	3.5	 **4d**	85
5	 **3e**	4	 **4e**	92
6	 **3f**	4	 **4f**	90
7	 **3g**	3.5	 **4g**	93
8	 **3h**	4	 **4h**	95

[a] Isolated yields after column chromatography.

Table 3
Tritylation of 3-phenylpropanol in the presence of different acid catalysts

Entry	Acid catalyst (3 mol %)	Time (h)	Yield[a] (%)
1	$BF_3{\cdot}Et_2O$	4	Complex mixture
2	$ZnCl_2$	5	86
3	$AlCl_3$	4	84
4	*p* TSA	4	88
5	I_2	4	74
6	$B(C_6F_5)_3$	3	92

[a] Isolated yield.

Deprotection of the trityl group, which is well known under acidic conditions,[16,32–34] was also attempted using the same catalyst [$B(C_6F_5)_3$] in methanol, but without success even at refluxing temperature.

In conclusion, we have demonstrated an extremely facile and efficient method for protection of alcohols as trityl ethers in the presence of 3 mol % of tris(pentafluorophenyl)borane. Using this procedure, primary alcohols were protected as trityl ethers in the presence of secondary alcohols under mild reaction conditions. The stability of acid-labile protecting groups is an added advantage of the method. In addition, the protocol offers the opportunity to install a trityl protecting group in the presence of base-sensitive functionalities such as esters.

General experimental procedure for the tritylation of alcohols: To a mixture of alcohol (1.0 mmol) and triphenylmethanol (1.5 mmol) in dichloromethane (5 mL), 3 mol % of $B(C_6F_5)_3$ was added and the reaction mixture stirred for the given time (see Tables 1 and 2). After completion of the reaction (monitored by TLC), the reaction mixture was diluted with dichloromethane (5 mL) and washed with water (1 × 5 mL) and brine (1 × 5 mL). The organic layer was dried over Na_2SO_4 and evaporated in vacuo. The crude compound was purified by column chromatography (hexanes and ethyl acetate) to afford the corresponding trityl ether.[35]

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.12.020.

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35. *Spectral data for representative products*: *(2S,3R,4S,5R)-2,3,4-Trimethoxy-5-(trityloxymethyl) tetrahydrofuran* (**2g**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49–7.43 (m, 6H), 7.33–7.19 (m, 9H), 5.85 (d, $J = 3.7$ Hz, 1H), 4.54 (d, $J = 3.7$ Hz, 1H), 4.37–4.30 (m, 1H), 3.78 (d, $J = 2.8$ Hz, 1H), 3.46–3.40 (m, 1H), 3.32 (s, 3H), 3.29–3.25 (m, 1H), 1.53 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.1, 128.6, 127.6, 127.1, 111.6, 105.1, 86.5, 84.0, 82.1, 81.8, 79.4, 61.0, 58.1, 27.3; IR (KBr): ν 3418, 1636, 1215, 757 cm^{-1}; HRMS-ESI calcd for $C_{28}H_{30}O_5Na$: 469.1990; found, 469.1992. *2-(2-(Benzyloxy)ethyl)-2-(2-(trityloxy)ethyl)-1,3-dioxolane* (**2i**): ^{1}H NMR (300 MHz, $CDCl_3$):

δ 7.48–7.38 (m, 8H), 7.34–7.14 (m, 12H), 4.47 (s, 2H), 3.88–3.68 (m, 4H), 3.54 (t, $J = 6.7$ Hz, 2H), 3.20 (t, $J = 6.7$ Hz, 2H), 2.03–1.87 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.5, 138.6, 128.8, 128.5, 127.9, 127.8, 127.6, 127.0, 109.6, 87.0, 76.3, 66.3, 65.3, 60.0, 43.9, 37.9; IR (KBr): ν 2985, 1374, 1242, 1099, 1047 cm^{-1}; HRMS-ESI calcd for $C_{33}H_{34}O_4Na$: 517.2354; found, 517.2352. *tert-Butyldimethyl(3-(trityloxy)propoxy)-silane* (**4b**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 (d, $J = 6.2$ Hz, 6H), 7.24 (m, 9H), 3.70 (t, $J = 6.2$ Hz, 2H), 3.15 (t, $J = 6.2$ Hz, 2H), 1.89–1.61 (m, 2H), 0.92 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 128.9, 127.8, 127, 86.6, 60.1, 59.9, 33.6, 26.1, 18.5, −5.12; IR (KBr): ν 3449, 2928, 1636, 1088, 836, 702 cm^{-1}; HRMS-ESI: calcd for $C_{28}H_{36}O_2NaSi$: 455.2376; found, 455.2386. *(3-(Methoxymethoxy)propoxy)triphenylmethane* (**4d**): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46–7.40 (m, 6H), 7.33–7.18 (m, 9H), 4.57 (s, 2H), 3.67 (t, $J = 6.7$ Hz, 2H), 3.29 (s, 3H), 3.17 (t, $J = 6.7$Hz, 2H), 1.96–1.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.5, 128.9, 128.1, 127.9, 127.4, 127.0, 96.6, 86.6, 65.3, 60.7, 55.3, 30.6; IR (KBr): ν 3019, 1215, 762, 670 cm^{-1}; HRMS-ESI calcd for $C_{24}H_{26}O_3Na$: 385.1774; found, 385.1775. See Supplementary data for spectral data of all the other new products.