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Tris(pentafluorophenyl)borane catalyzed acylation of alcohols, phenols, amines, and thiophenols under solvent-free condition

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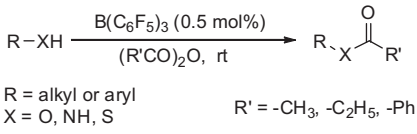
ABSTRACT

The acylation of alcohols, phenols, amines, and thiophenols was accomplished with 0.5 mol % of tris (pentafluorophenyl)borane [$B(C_6F_5)_3$] at ambient temperature under solvent-free condition. Major advantages of this method include high yield, short reaction time, simple procedure, compatibility with sensitive protecting groups as well as other functional groups, absence of racemization of optical active compounds, and epimerization of sugars.

Acylation of alcohols, phenols, and amines are one of the most important manipulation in synthetic chemistry, which serve as imperative synthetic intermediate especially in the synthesis of polyfunctional molecules such as nucleoside, natural products, and carbohydrates. Acylation is a very frequently employed organic transformation in multistep organic synthesis because of the affluence of accession as well as mild condition for de-protection. Usually, anhydrides and acid chlorides are the most commonly used acyl source to achieve acylated product either in the presence of acid or base. The deprived nucleophilic properties of hydroxylic compounds, particularly phenols, need activation of anhydrides. A wide range of activators engaged for this purpose include various reagents such as DMAP,[1] Et_3N,[2] pyridine,[2] 4-pyrrolidinopyridine (PPY),[3] and Bu_3P.[4] A variety of other catalysts such as $TaCl_5$,[5a] $ErCl_3$,[5-b] $CoCl_2$,[6] $ZnCl_2$,[7a] ZnO,[7b,c] HBF_4-SiO_2,[8a] $ZrCl_4$,[8b,c] $LiClO_4$,[8d,e] Ru-catalysts,[8f] $Mg(ClO_4)_2$,[8g] SmI_2,[9a] $Sm(O\text{-}Tf)_3$,[9b] $CeCl_3$,[9c] $ZrOCl_2{\cdot}8H_2O$,[9d] montmorillonite,[9e] TMS-Cl,[9f] PTSA,[10a] distannoxane,[10b] ionic liquids,[10c], I_2,[10d,e] $La(O^iPr)_3$,[11a] $La(NO_3)_3{\cdot}8H_2O$,[11b] vanadyl(V)acetate,[11c] solid supported reagents,[11d] lipase enzymes,[11d] and various triflates[12a–f] have been used for the acylation of alcohols. Acylations with acids,[13a,b] acyl imidazoles,[13c] and acyl urea[13d] are also known. Recently, a variety of new acylation catalysts appeared, for example pentafluorophenylammonium triflate,[14a] silica magnesium oxide,[14b] polyvinylpolypyrrolidone-bound boron trifluoride,[14c] *N*-acyl 1,5-diazabicyclo [4.3.0] non-5-ene tetraphenylborate salts,[14d] and iron(III)tosylate,[14e] and TfOH.[14f]

Despite the great importance of the above procedure in organic syntheses, it has major drawbacks such as stoichiometric or super stoichiometric amounts of a Lewis acid or Bronsted acid, stringent conditions, long reaction time, formation of side products, cumbersome methodology, incompatibility with other functional groups, use of halogenated solvent, and excess of acylating agents, use of hazardous materials (e.g. DMAP is highly toxic,[14g] Bu_3P is highly flammable and air sensitive[14h]), special effort to prepare the catalysts (e.g. $Sc(NTf_2)_3$, Nafion-H, yttria zirconia,) and in most of the cases being applicable to alcohols only. Hence, the development of a more general, efficient, and environmentally benign catalytic methodology is still of practical importance.

The ongrowing acquaintance on assorted issues accompanying environment abuse ascendancy has led to the search for more affable forms of catalysts that display less or no-toxicity to human health and environment.[15] Tris(pentafluorophenyl)borane [$B(C_6F_5)_3$] has received considerable attention as non-conventional, nontoxic, air-stable, water-tolerant, and thermal abiding Lewis acid.[16a] Recently, various research groups were engaged in exploring the impending efficacy of $B(C_6F_5)_3$ for various organic transformations, such as ring-opening of epoxides, aza-Ferrier



Scheme 1. General scheme for acylation of alcohols, phenols, amines, and thiophenols.

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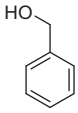
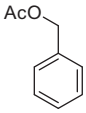
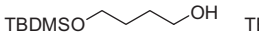
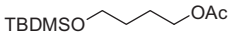
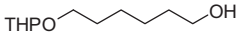
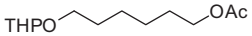
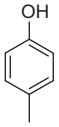
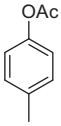
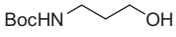
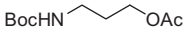
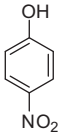
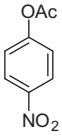
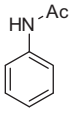
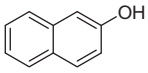
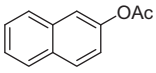
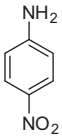
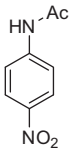
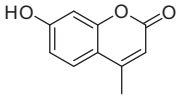
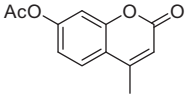
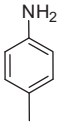
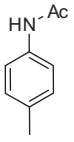
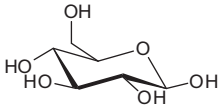
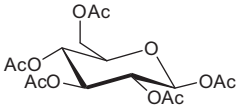
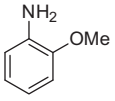
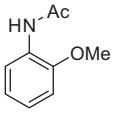
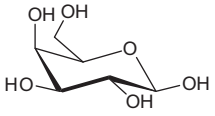
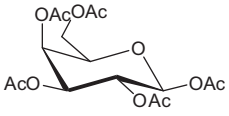
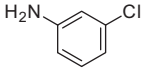
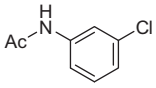
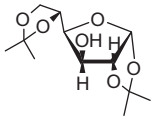
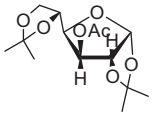
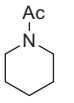
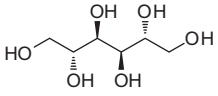
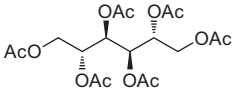
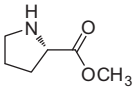
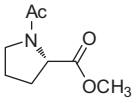
0040-4039/

Table 1
$B(C_6F_5)3$ catalyzed acylation of alcohol, phenol, thiophenol, and amine[a]

Entry	Substrate	Product	Time (min)	Yields[b]	Entry	Substrate	Product	Time (min)	Yields[b]
1[12f,14d]			2	98	14[11b]			2	94
2[12f,14d]			15	92	15[11b]			2	92
3[12f]			13	95	16[8c]			2	90
4[9b]			15	93	17[11b]			1	96
5[14e]			20	98[c]	18[11b]			2	97
6[8e]			8	95[c]	19[13b]			1	98
7[10d]			20	94[c]	20[13c]			1	95
8[10d]			20	92[c]	21[13b]			1	95
9[10d]			3	93[c]	22[13b]			1	97
10[9c,12f]			15	96[c]	23[19]			3	91
11[9c,12f]			2	96	24[19]			2	94
12[12g]			2	97	25[9c,12f]			30	92
13[14e]			3	95	26[9c,12f]			35	90

[a] All reactions were performed by using 0.5 mol % catalyst, 1.2 equiv of acetic anhydride.
[b] Isolated yields.
[c] Excess of acetic anhydride used.

glycosylation,[16b–d] hydrosilylation of imines,[16e] reduction of alcohols with silane,[16f] and hydrogenation of imines,[16g] Friedel–Crafts reactions between activated arenes or heteroarenes and α-amidosulfones,[16h] Sakurai allylation.[16i] In this perception, $B(C_6F_5)_3$ has been utilized to catalyze the regio- and stereoselective cyclizations of unsaturated alkoxysilanes.[17a] $B(C_6F_5)_3$ is also an efficient activator for polymethylhydrosiloxane in the reduction of different functional groups.[17b,c]

Herein, we wish to report a mild and efficient method for the acylation of alcohols, phenols, amines, and thiophenols with acetic anhydride, using a catalytic amount of $B(C_6F_5)_3$ under solvent-free conditions (Scheme 1).

In a test reaction, 1 mmol of benzyl alcohol was treated with 1.2 mmol of Ac_2O in the presence of $B(C_6F_5)_3$ (0.5 mol %) at room temperature. The completion of reaction was monitored by TLC, in which the complete disappearance of starting material was observed in 2 min and yielded 98% of acylated product (Table 1, entry 1). Encouraged by the success of this reaction various primary, secondary, and cyclic alcohols were subjected to acylation in excellent yields under similar reaction conditions.[18] To explore the simplification and scope further, $B(C_6F_5)_3$ catalyzed acylation was examined using other structurally diverse phenols, amines, and thiols and the results are summarized in Table 1.

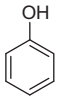
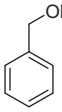
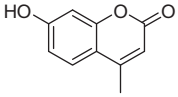
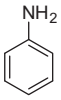
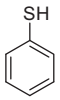
Phenolic compounds were efficiently acetylated (entries 2–5) but required prolonged reaction time than alcohols due to their relatively poor nucleophilicity. Phenolic compounds containing both electron donating (entry 3) and electron withdrawing (entry 4) reacted equally efficiently under present reaction conditions. Similarly, β-naphthol (entry 5) and 7-hydroxy coumarin (entry 6) were also converted into corresponding acetate, in excellent yields without any side products.

Furthermore, sugars were also subjected to O-acylation using an excess of acetic anhydride and 0.5 mol % of $B(C_6F_5)_3$ to afford fully acetylated products in quantitative yields (entries 7–10). Moreover, racemization or epimerization was not observed to any extent in the acetylated products, when stereogenic centers were present in the substrates. Cyclohexanol (entry11), and cyclopentanol (entry 12), were all promptly acylated to afford corresponding acetates under similar reaction conditions.

Similarly, acylation of *l*-menthol was carried out without any detrimental effect on optical purity. It is noteworthy that acid sensitive functional groups such as TBDMS, THP, and Boc can survive in the present method, demonstrating the mildness of the acylation process (entries 14–16). Interestingly, extension of the present methodology to various amines and thiophenols furnished corresponding acylated product in excellent yields. The reaction of amines with acetic anhydride was so fast in comparison to that of alcohols (entries 17–22). In case of aromatic amines, there was no significant influence of electron donating or electron withdrawing substituents and reacted equally efficiently under the standard reaction conditions. Consequently, the reaction of methyl ester of L-proline and L-phenyl alanine with acetic anhydride in the presence of 0.5 mol % of $B(C_6F_5)_3$ afforded the desired products in 91% and 94% yields respectively without any disturbance on chirality (entries 23–24). Finally, the reactions of thiophenol and mercapto cyclohexane were slow under present reaction conditions. However, acetates of thiophenol and mercaptocyclohexane were achieved in 92% and 90% yields respectively (entries 25–26).

As a logical extension of this methodology, we further investigated the efficiency of $B(C_6F_5)_3$ as a catalyst for propionylation and benzoylation using propionic anhydride and benzoic anhydride respectively (Table 2). To our delight all the studied substrates such as benzyl alcohol, phenols, cyclohexanol, aniline, and thiophenol were successfully provided corresponding propionylated and benzoylated products in excellent yields as tabulated in Table 2.

Table 2
$B(C_6F_5)_3$ catalyzed acylation, benzoylation, and propionylation of alcohol, phenol, amine, and thiophenol[a]

Entry	Substrate	Acylating agent	Time (min)	Yields[b]
1[14f]		Propionic anhydride	5	96
		Benzonic anhydride	15	94
2[5b,7b]		Propionic anhydride	1	98
		Benzonic anhydride	10	95
3[20]		Propionic anhydride	4	97[c]
		Benzonic anhydride	15	95[c]
4[10e,7c]		Propionic anhydride	4	98
		Benzonic anhydride	10	96
5[21,7b]		Propionic anhydride	2	96
		Benzonic anhydride	15	94
6[22]		Propionic anhydride	25	92
		Benzonic anhydride	45	90

[a] All reactions were performed by using 1.2 equiv of acylating agent.
[b] Isolated yields.
[c] Excess of acylating agent used.

In summary, we have demonstrated that tris(pentafluorophenyl) borane is an extremely facile and efficient catalyst for acylation, benzoylation, and propionylation of alcohols, phenols, amines as well as thiophenols. The advantages of this method are environmental benign, low catalyst loading, non toxic catalyst, solvent-free condition, rapid reaction, high yields of the desired products, and simple experimental procedure. In addition, chirality retention, and tolerance of acid labile protecting groups such as TBDMS, THP, and Boc are an added advantage of the present method.

An established 'Lewis acid assistance' mechanism holds good for this strategy considering that coordination of carbonyl oxygen with $B(C_6F_5)_3$ results in partial charge-transfer character, which makes the lone-pair donor effectively more electronegative and enhances the electrophilicity of acylating agents toward nucleophilic attack.

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References and notes

1. (a) Litvinenko, L. M.; Kirichenko, A. I. *Dokl. Akad. Nauk SSSR, Ser. Khim.* **1967**, *176*, 97; (b) Steglich, W.; Höfle, G. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 981.

2. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: NY, 1999.
3. Hofle, G.; Steglich, V.; Vorbruggen, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569.
4. Vedejs, 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.
5. (a) Chandrasekhar, S.; Ramchander, T.; Takhi, M. *Tetrahedron Lett.* **1998**, *39*, 3263; (b) Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Oliverio, M.; Procopio, A.; Russo, B.; Tocci, A. *Aust. J. Chem.* **2007**, *60*, 75.
6. Iqbal, J.; Srivastava, R. R. *J. Org. Chem.* **2001**, *1992*, 57.
7. (a) Backer, R. H.; Bordwell, F. G. *Org. Synth.* **1955**, *3*, 141; (b) Sarvari, M. H.; Sharghi, H. *Tetrahedron* **2005**, *61*, 10903; (c) Tamaddon, F.; Amrollahi, M. A.; Sharafat, L. *Tetrahedron Lett.* **2005**, *46*, 7841.
8. (a) Chakraborti, A. K.; Gulhane, R. *Tetrahedron Lett.* **2003**, *44*, 3521; (b) Chakraborti, A. K.; Gulhane, R. *Synlett* **2004**, 657; (c) Reddy, C. S.; Smitha, G.; Chandrasekhar, S. *Tetrahedron Lett.* **2003**, *44*, 4693; (d) Nakae, Y.; Kusaki, I.; Sato, T. *Synlett* **2001**, 1584; (e) Rajabi, F.; Saidi, M. R. *Synth. Commun.* **2005**, *35*, 483; (f) Martin-Matute, B.; Edin, M.; Bogar, K.; Backvall, J. E. *Angew. Chem., Int. Ed.* **2004**, *43*, 6535; (g) Bartoli, G.; Bosco, M.; Dalpozzo, R.; Marcantoni, E.; Massaccesi, M.; Rinaldi, S.; Sambri, L. *Synlett* **2003**, 39.
9. (a) Ishii, Y.; Takeno, M.; Kawasaki, Y.; Muromachi, A.; Nishiyama, Y.; Sakaguchi, S. *J. Org. Chem.* **1996**, *61*, 3088; (b) Roy, B.; Dasgupta, S.; Kumar Rajput, V.; Mukhopadhyay, B. *J. Carbohydr. Chem.* **2008**, *27*, 1; (c) Torregiani, E.; Gianfranco, S.; Minassi, A.; Appendino, G. *Tetrahedron Lett.* **2005**, *46*, 2193; (d) Ghosh, R.; Swarupananda, M.; Chakraborty, A. *Tetrahedron Lett.* **2005**, *46*, 147; (e) Li, A.-I.; Li, T.-S.; Ding, T.-H. *Chem. Commun.* **1997**, 1389; (f) Kumareswaran, R.; Gupta, A.; Vankar, Y. D. *Synth. Commun.* **1997**, *27*, 277.
10. (a) Cope, A. C.; Herrick, E. C. *Org. Synth.* **1963**, *4*, 304; (b) Orita, A.; Sakamoto, K.; Hamada, Y.; Mitsutome, A.; Otera, J. *Tetrahedron* **1999**, *55*, 2899; (c) Lee, S. G.; Park, J. H. *J. Mol. Catal. A: Chem.* **2003**, *194*, 49; (d) Kartha, K. P. R.; Field, R. A. *Tetrahedron* **1997**, *53*, 11753; (e) Jereb, M.; Vrazic, D.; Zupan, M. *Tetrahedron Lett.* **2009**, *50*, 2347.
11. (a) Hatano, M.; Furuya, Y.; Shimmura, T.; Moriyama, K.; Kamiya, S.; Maki, T.; Ishihara, K. *Org. Lett.* **2011**, *13*, 426; (b) Reddy, T. S.; Narasimhulu, M.; Suryakiran, N.; Mahesh, K. C.; Ashalatha, K.; Venkateswarlu, Y. *Tetrahedron Lett.* **2006**, *47*, 6825; (c) Choudary, B. M.; Kantam, M. L.; Neeraja, V.; Bandyopadhyay, T.; Reddy, P. N. *J. Mol. Cat.: A Chem.* **1999**, *140*, 25; (d) Berger, B.; Rabiller, D. G.; Konigsberger, K.; Faber, K.; Griengl, H. *Tetrahedron: Asymmetry* **1991**, *1*, 541.
12. (a) Orita, A.; Tanahashi, C.; Kakuda, A.; Otera, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2877; (b) Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1995**, *117*, 4413; (c) Ishihara, K.; Kubota, M.; Yamamoto, H. *Synlett* **1996**, 265; (d) Procopiou, P. A.; Baugh, S. P. D.; Flack, S. S.; Inglis, G. G. A. *J. Org. Chem.* **1998**, *63*, 2342; (e) Chauhan, K. K.; Frost, C. G.; Love, I.; Waite, D. *Synlett* **1999**, 1743; (f) Kamal, A.; Khan, M. N. A.; Reddy, K. S.; Srikanth, Y. V. V.; Krishnaji, T. *Tetrahedron Lett.* **2007**, *48*, 3813; (g) Khaligh, N. G. *J. Mol. Catal. A: Chem.* **2012**, *363*, 90.
13. (a) Ishihara, K.; Nakayama, M.; Ohara, S.; Yamamoto, H. *Tetrahedron* **2002**, *58*, 8179; (b) Prasad, H. S.; Srinivasa, G. R.; Channe Gowda, D. *Synth. Commun.* **2005**, *35*, 1189; (c) Kamijo, T.; Harada, H.; Iizuka, K. *Chem. Pharm. Bull.* **1984**, *32*, 2560; (d) Dhanon, M. K.; Olsen, R. K.; Ramaswamy, K. *J. Org. Chem.* **1962**, *1982*, 47.
14. (a) Samad, K.; Hasan, Z. *Comb. Chem. High Throughput Screening* **2012**, *15*, 1875; (b) Ghosh, P.; Mandal, A. *J. Ind. Chem. Soc.* **2012**, *89*, 261; (c) Mokhtary, M.; Qandalee, M.; Najafizadeh, F. C. R. *Chimica* **2012**, *15*, 389; (d) Taylor, J. E.; Williams, J. M. J.; Bull, S. D. *Tetrahedron Lett.* **2012**, *53*, 4074; (e) Baldwin, N. J.; Nord, A. N.; O'Donnell, B. D.; Mohan, R. S. *Tetrahedron Lett.* **2012**, *53*, 6946; (f) Murashige, R.; Hayashi, Y.; Ohmori, S.; Torii, A.; Aizu, Y.; Muto, Y.; Murai, Y.; Oda, Y.; Hashimoto, M. *Tetrahedron* **2011**, *67*, 641; (g) Sweet, D. V. *In Registry of Toxic Effects of Chemical Substances*; US Government Printing Office: Washington, DC, 1988. Vol. 1985–1986, p 3336; (h) Buckler, S. A. *J. Am. Chem. Soc.* **1962**, *84*, 3093.
15. Anastas, P.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University: Oxford, 1998.
16. (a) Blackwell, J. M.; Piers, W. E.; Parvez, M. *Org. Lett.* **2000**, *2*, 695; (b) Chandrasekhar, S.; Reddy, C. R.; Babu, B. N.; Chandrashekar, G. *Tetrahedron Lett.* **2002**, *43*, 3801; (c) Chandrasekhar, S.; Reddy, C. R.; Chandrashekar, G. *Tetrahedron Lett.* **2004**, *45*, 6481; (d) Srihari, P.; Yaragorla, S. R.; Basu, D.; Chandrasekhar, S. *Synthesis* **2006**, 2646; (e) Gevorgyan, V.; Rubin, M.; Benson, S.; Liu, J.; Yamamoto, Y. *J. Org. Chem.* **2000**, *65*, 6179; (f) Blackwell, J. M.; Sonmor, E. R.; Scoccitti, T.; Piers, W. E. *Org. Lett.* **2000**, *2*, 392; (g) Chen, D.; Klankermayer, J. *Chem. Commun.* **2008**, 2130; (h) Thirupathi, P.; Neupane, L. N.; Lee, K. H. *Tetrahedron* **2011**, *67*, 7301; (i) Thirupathi, P.; Neupane, L. N.; Lee, K. H. *Bull. Korean Chem. Soc.* **2012**, *33*, 1275.
17. (a) Shchepin, R.; Xu, C.; Dussault, P. *Org. Lett.* **2010**, *12*, 4772; (b) Chandrasekhar, S.; Reddy, C. R.; Babu, B. N. *J. Org. Chem.* **2002**, *67*, 9080; (c) Chandrasekhar, S.; Chandrashekar, G.; Vijeender, K.; Reddy, M. S. *Tetrahedron Lett.* **2006**, *47*, 3475.
18. *Typical experimental procedure:* $B(C_6F_5)_3$ (0.5 mol %) was added to a mixture of alcohol/phenol/thiophenol/amine (1 mmol) and acetic anhydride (1.2 mmol), and the reaction mixture was stirred at room temperature until the complete conversion of starting material (monitored by TLC). After completion of reaction, the reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3×15 mL). The organic layer was washed with cold saturated sodium bicarbonate solution (2×20 mL) followed by brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure and products were purified over silica gel column chromatography in ethyl acetate/hexane. All compounds were characterized and confirmed by comparison of their spectral data and physical properties with reported literature.
19. Gibson, S.; Romero, D.; Jacobs, H. K.; Gopalan, A. S. *Tetrahedron Lett.* **2010**, *51*, 6737.
20. (a) Kumar, A.; Sharma, S.; Gupta, L. P.; Ahmad, P.; Srivastava, S. P.; Rahuja, N.; Tamrakar, A. K.; Srivastava, A. K. *Bioorg. Med. Chem.* **2012**, *20*, 2172; (b) Babiak, P.; Reymond, J.-L. *Anal. Chem.* **2005**, *77*, 373.
21. Metz, P.; Mues, C. *Tetrahedron* **1988**, *44*, 6841.
22. Ahmad, S.; Iqbal, J. *Tetrahedron Lett.* **1986**, *27*, 3791.