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Title Key: An efficient method for the *S*-alkylation …

An efficient method for the *S*-alkylation of thiols with alcohol catalyzed by 3-nitrobenzene boronic acid under environmentally benign conditions.

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Abstract

The 2.5 mol % of 3-nitrobenzene boronic acid was found to be an effective catalyst for s-alkylation of thiols with alcohol under mild, environmentally benign and solvent free condition.

Keyword: Thioether, alkylating agents, Mitsunobu type reactions.

Introduction

Versatile applications of thioether in both organic and bioorganic chemistry have ensured many studies of their preparation by different methods. The thioether linkage has been used to prepare cyclic analogues of acyclic polypeptides to restrict their conformational mobility and thus increase their biological activity and stability against biodegradation.[1-4] They are also useful heteroatomic functional groups inorganic synthesis, for example, by oxidation of thioethers, chiral sulfoxides can be generated which can be used as auxiliaries, in asymmetric synthesis.[5-8] Moreover, sulfones have been employed for stabilizing α-radicals,[9] α-anions,[10] can act as cationic synthons,[11] and also for the formation of c-c bonds.[12]

A variety of methods are available for the preparations of thioethers, such as, deoxygenations of sulfoxides,[13-14] displacement of leaving groups with sulfur nucleophiles,[15-16] addition of thiols to carbonyl compounds followed by in situ reduction of the generated intermediate thionium ion,[17] anti-Markownikov addition of alkene and alkane thiols to alkenes,[18-19] Mitsunobu type reactions,[20-24] metal-mediated cross-coupling process,[25-27] and metal catalyzed hydrothiolation of alkynes.[28] These reported methods have been recently reviewed.[29-30]

However, in the majority of cases reported, the thioethers have been prepared using expensive and commercially unavailable materials.[23-26] hazardous and corrosive compounds such as, alkylating agents,[24] strong reducing agents,[17] harsh reaction conditions and involve tedious work-up procedures.[29-30] Additionally, some of the reported methods can not be used for the preparation of different structurally and electronically diverse thioethers. For example, by applying modified Mitsunobu conditions using liquid trimethylphosphine combined with 1,1'-(azodicarbonyl)-dipiperidine (a hazardous material) in the presence of imidazole, aliphatic thiols react only with

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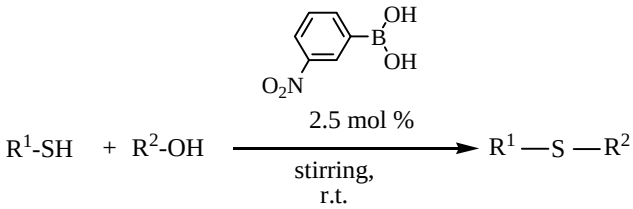
primary alcohols to give thioethers, other types of thiols and alcohols did not react[20]

Result and Discussion

In continuation of our interest in exploring applications of 3-nitrobenzene boronic acid[35] to make the process environmentally benign and to avoid organic solvents used in chemical processes, much attention has been devoted to the use of an alternatives reaction media. Besides the use of supercritical fluids, water, ionic liquids and the possibly of performing chemical processes under solvent free conditions has been received more attention [29, 30]. Since organic sulfur compounds have become increasingly useful and important in organic synthesis, the developments of convenient and efficient protocol for the preparation of appropriate sulfides which carry other functional groups are in high demand. The leading contender for an environmentally acceptable alternative is the utility of 3-nitro benzene boronic acid as versatile Lewis acid catalyst. The strong potential of these catalyst is evident from the fact that the turn over number up to 1000 can be achieved Increasingly chemists are looking for cleaner and environmentally benign ways to make target molecules Consequently the solvent less protocol with environmentally friendly benign reagents provides an excellent tool for achieving environmentally solvent less organic synthesis. Interest in developing true catalyst using in expensive and non-polluting reagent, we wish to report 3-nitro benzene boronic acid [31] promoted s-alkylation of alcohol with thiols at room temperature under solvent free conditions (Scheme –I)



Scheme – I

In order to optimize the reaction conditions, condensation of benzyl alcohol with 4-methylthiophenol was studied as a model reaction in the presence of 3-nitro benzene boronic acid, we observed that a sticky reaction mixture was obtained with the formation of the corresponding thiother in around 50-60% yield. Increasing the reaction time did not affect the yield of the product. We found that using benzyl alcohol (1mmol), 4-methyl thiophenol (1.1 mmol) and 3-nitro benzene boronic acid (2.5 mol%) in the absence of solvent, the reaction proceed very cleanly at room temperature and corresponding thioether was isolated in 94% yield.

We found that this method applicable for the preparation of thioethers from the reaction of cinnamyl alcohol, adamantanol structurally and electronically diverse benzyl alcohols with aromatic or aliphatic thiols and also with dithiols.[35,36] we noted that electronic factors play a role in these reactions. Aromatic alcohols substituted with electro donating groups reacted faster than those substituted with electron with drawing groups and also provided the thiothers in higher yields (table1, entries 6-9). This method is also useful for the high yielding preparation of dithioether using dithiols (table 1, entry 23 and 24). We have also used this method for the efficient preparation of dithioethers[37], (table 1, and entry 35) which could be used as precursors for the

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preparation of macro cyclic or polymeric sulfur containing compounds.

Primary and secondary aliphatic alcohols do not react with thiols in the presence of this reagent and remain mostly intact after the typical reaction times (table1, entries 15 and 16).

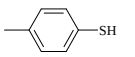
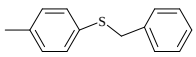
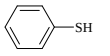
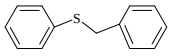
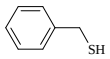
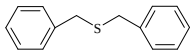
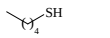
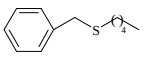
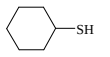
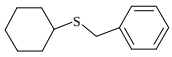
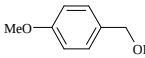
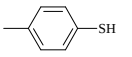
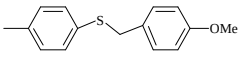
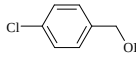
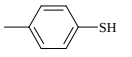
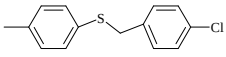
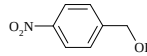
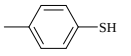
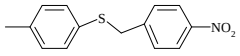
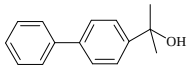
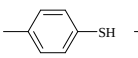
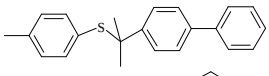
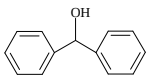
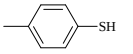
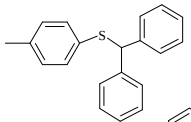
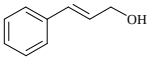
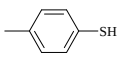
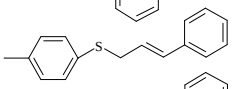
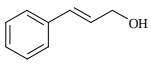
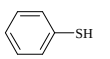
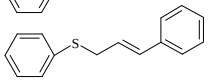
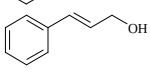
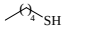
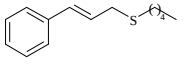
Generation of a classical carbocation is improbable in these reactions. Adamantanol because of its structure does not allow the generation of a classical carbocation (table 1, entry 18). In addition the reaction of 2-(4-biphenyl-4-yl)-2-propanol [table 1, entry 9] was not accompanied by the production of it's corresponding olefin as an elimination by product the low yield and the rather slow rate of the reaction involving 4-nitrobenzyl alcohol is an indication of the generation of an unstable partially positively charged intermediate (table1, entry 8).

General experimental procedure

All reactions are carried out using 3-nitrobenzene boronic acid at room temperature. All solvent and reagents were purified before use.

To a mixture of thiols (1.1 mmol) and various substituted alcohols (1mmol) 3-nitrobenzene boronic acid was added (2.5 mol %) and stir the reaction mixture at room temperature. The reaction was monitored by TLC after completion of reaction product was extracted with diethyl ether removal of this solvent under vaccum furnished crude product, which was further purified by column chromatography using silica gel (mesh – 100-200) and pet ether: ethyl acetate (9:1)

Table : S-Alkylation of thiols with alcohols using 3-Nitrobenzene boronic acid under solvent-free conditions.[a]

Entry	Alcohol	Thiol	Product[b]	Time (min)	Yield (%)
1				5	94
2				1	90
3				3	53
4				2	70
5				1	89
6				2	94
7				2	94
8				4	50
9				4	95
10				3	95
11				5	95
12				12	92
13				8	90

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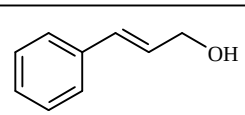
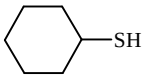
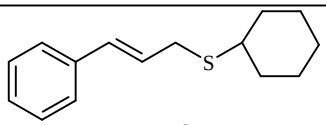
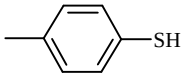
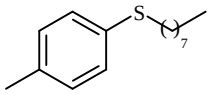
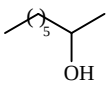
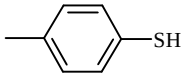
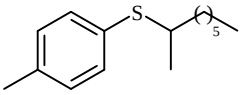
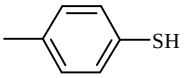
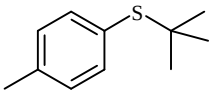
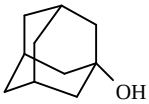
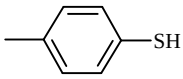
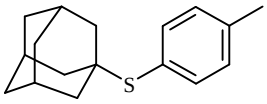
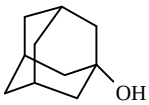
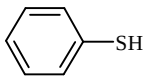
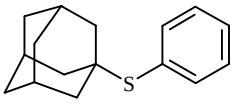
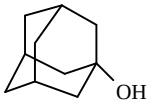
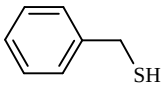
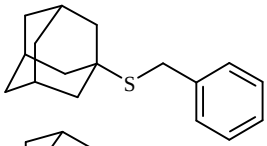
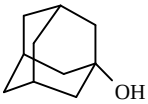
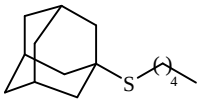
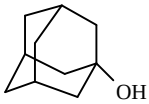
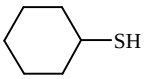
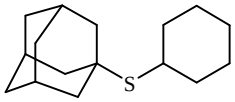
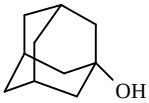
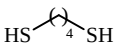
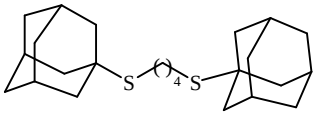
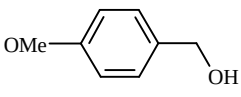
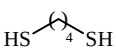
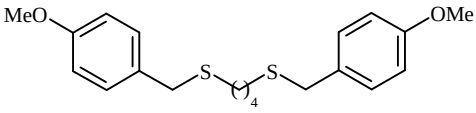
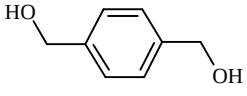
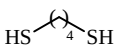
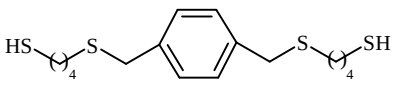
Entry	Alcohol	Thiol	Product[b]	Time (min)	Yield (%)
14				5	90
15				180	---
16				180	---
17				10	80
18				7	94
19				10	96
20				30	95
21				15	94
22				15	95
23				20	95
24				10	96
25				20	94

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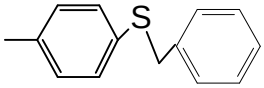
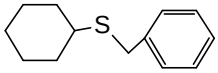
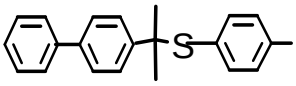
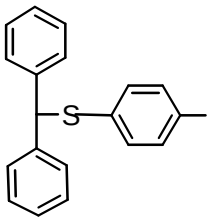
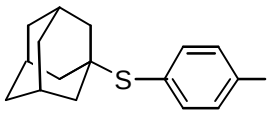
Spectral data of new compounds

Structure	MS	^{1}H NMR ($CdCl_3$)
	m/z = 214 (M^+)	δ = 2.28 (s, 3H), 4.05 (s, 2H), 7.10-7.68 (m, 9H)
	m/z = 206 (M^+)	δ = 0.82 (m, 6H), 1.33 (m, 4H), 1.55 (m, 1H), 4.19 (s, 2H)
	m/z = 318 (M^+)	δ = 1.69 (s, 6H), 2.29 (s, 3H), 6.97-7.69 (m, 13H)
	m/z = 290 (M^+)	δ = 2.23 (s, 3H), 4.56 (s,1H), 7.10-7.46 (m, 14H)
	m/z = 258 (M^+)	δ = 1.47 - 1.99 (m, 15H), 2.35 (s, 3H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H)

Conclusion

We report an environmentally friendly, simple, convenient and highly efficient method for the regioselective s-alkylation (thioether) using thiols with alcohols under solvent free conditions using an in expensive and friendly benign catalyst. The salient features of the present protocol are mild reaction conditions, greater regioselectivity, cleaner reaction profile, excellent yields with experimental simplicity, which makes it potentially useful for the industrial application.

References

i . Moberg. H. I.; Omnaas, J. R. *J. Am. Chem. Soc*. 107, 2986-2987.
ii. Hurby, V. J.; Al-Obeidi, F.; Kazmierski, W. Biochem **1990,** 268, 249-262.
iii. Kataoka, T.; Beusen, D. D.; Clar, J. D.; Yodo, Marshall, G. R. Biopolymers **1992,** 32, 1519-1533.

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iv. Hurby, V. J.; Bonner, G. G. *Methods Mol. Biol*. **1994.** 201-240.
v. Solladie, G. *Synthesis* **1981**, 185-196.
vi. Posner, G. H. In The Chemistry of Sulfones and Sulfox Patai S., Rappoport, Z., Sterling, C. J. M., Eds.; We Chichester, **1988**, Chapter 16.
vii. Mata, E. G. *Phosphorus, Sulfur Silicon* **1996**, 117, 286.
viii. Carreno, M. C. *Chem. Rev*. **1995**, 95, 1717-1760.
ix. Paquette, L. A. *Synlett* **2001**, 1-12.
x. Najera, C.; Sansano, J. M. *Recent Res. Develop. Chem*. **1998**, 2, 637-683.
xi. Chinchila, R.; Najera, C. *Recent Res. Develop. Org* **1997**, 1, 437- 467.
xii. Yao, Q. *Org. Lett* **2002,** 4, 427-430.
xiii. Madesclaire, M. *Tertrahedron* **1988**, 44, 6537-6580.
xiv. Nicolaou, K. C.; Koumbis, A. E.; Snyder, S. A.; ;Simsen, K. B. *Angew. Chem., Int. Ed*. **2000**, 39, 2529-2533
xv. Zaragoza, F.; Stephensen, H. *Angew. Chem., Int. Ed*, 39, 554-556.
xvi. Dowsland, J.; Mckerlie, F.; Procter, D. J. *Tetrahedron Lett*. **2000**, 41, 4923-4927.
xvii. Procter, D. J.; Archer, N. J.; Needham, R. A.; Bell, Marchington, A. P.; Rayner, C. M. *Tetrahedron* **1999**, 9611-9622.
xviii. Kumar, P.; Pandey, P. K.; Hedge, V. R. *Synlett* .
xix. Chelucci, G.; Culeddu, N.; Saba, A.; Valenti, R. *Tetrahedron: Asymmetry* **1999**, 10, 3537-3546.
xx. Falck, J. R.; Lai, J. –Y.; Cho, S. –D.; Yu, J *Tetrahedron Lett*. **1999**. 40, 2903-2906.
xxi. Garofalo, A.; Campiani, G.; Fiorini, I.; Nacci, V. *Tetrahedron* **1999,** 55, 1479-1490.
xxii. Shibata, K.; Yamaga, H.; Misunobu, O. *Heterocycles* **1999**, 50, 947-968.
xxiii. Palomo, C.; Oiarbide, M.; Lopez, R.; Gomez-Bengo *Tetrahedron Lett*. **2000**, 41, 1283-1286.
xxiv. Herradura, P. S.; Pendola, K. A.; Guy, R. K. *Org. Lett.* **2000,** 2, 2019-2022.
xxv. Wendeborn, S.; De Mesmaeker, A.; Brill, W. K. Berteina, S. *Acc. Chem. Res.* **2000**, 33, 215-224.
xxvi. Savarin, C.; Srongl, J.; Liebeskind, L. S. *Org. Lett*. **2002** 4309-4312.
xxvii. Ogawa, A.; Ikeda, T.; Kimura, K.; Hirao, T. *J. Am Soc*. **1999,** 121, 5108-5114.
xxviii. Procter, D. J. J. *Chem. Soc., Perkin Trans*. 1 **2000,** 871.
xxix. Procter, D. J. J. *Chem. Soc. Perkin Trans*. 1. **2001.** 354.
xxx. Firotabadi, H.; Iranpoor, N.; Karii, B. *Synlett* **1999,** 319-320.
xxxi. Firouzabadi, H.; Iranpoor, N.; Karimi, B. *Synlett* **1999,** 321-323.
xxxii. Firouzabadi, H.; Iranpoor, N.; Jafarpour, M. *Tetrahedron Lett*. **2004,** 45, 7451-7454.
xxxiii. Firouzbadi, H.; Iranpoor, N.; Jafarpour, M. *Tetrahedron Lett*. **2005,** 46, 4107-4110.
xxxiv. R. H. Tale, R. N. Adude, *Tetrahedron Lett.* 2006, 47, 7263.
xxxv. P.Tundo, P.T.Anastas, green chemistry: Theory and practice, *Oxford-University Press*, Oxford**, 1998.**
xxxvi. K.Tanaka, F. Toda, solvent free organic synthesis, *Wiley-VCH*, **2003**.
xxxvii. A.K. Chakraborty, R. Gullhane, *Tetrahedron Lett.* 44 **2003,** 352.
xxxviii. Zaragoza, F. *Tetrahedron* **2001**, 57. 5451-5454.