

Tetrabutylammonium phthalimide-*N*-oxyl (TBAPINO) as an efficient, safe and recoverable catalyst for rapid trimethylsilyl protection of hydroxyl groups

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Abstract

Tetrabutylammonium phthalimide-*N*-oxyl (TBAPINO) can be used as an efficient organocatalyst for the conversion of alcohols to their corresponding trimethylsilyl ethers with hexamethyldisilazane (HMDS). All reactions were performed under mild and completely homogeneous reaction conditions in high to quantitative yields.

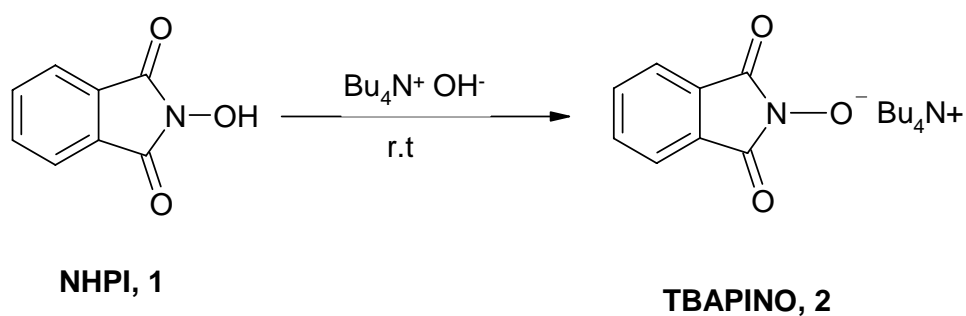
Introduction

Protection of hydroxyl groups is a common practice in synthetic organic [1] and analytical chemistry [2,3]. Many multistep syntheses and chemical transformations involve at least one step of hydroxyl group protection [4]. Conversion of alcohols into their corresponding trimethylsilyl ethers is perhaps the most popular strategy for this purpose [5]. In this context, 1,1,1,3,3,3-hexamethyldisilazane (HMDS) has emerged as the most versatile reagent in recent years for trimethylsilyl (TMS) protection of alcohols and phenols. Commercial availability, ease of handling, use of mild conditions, formation of ammonia as the only byproduct, [6] and convenient work-up are among the advantages of HMDS over traditional trimethylsilyl chloride or triflate reagents. [7] However, the poor silylation power is the main drawback for application of HMDS [8]. This limitation dictates the use of harsher reaction conditions and longer time periods. Several catalytic systems have been developed to facilitate HMDS silylation processes by using extra additives [9], microwave irradiation [10], solid phase synthesis [11], ultrasound activation [12], ionic liquid mediation [13] and Lewis acid catalysis [14–18].

Herein, we would like to present application of tetrabutylammonium phthalimide-*N*-oxyl (TBAPINO) as an efficient and safe organocatalyst for preparation of the title compounds under mild conditions (**Scheme 2**).

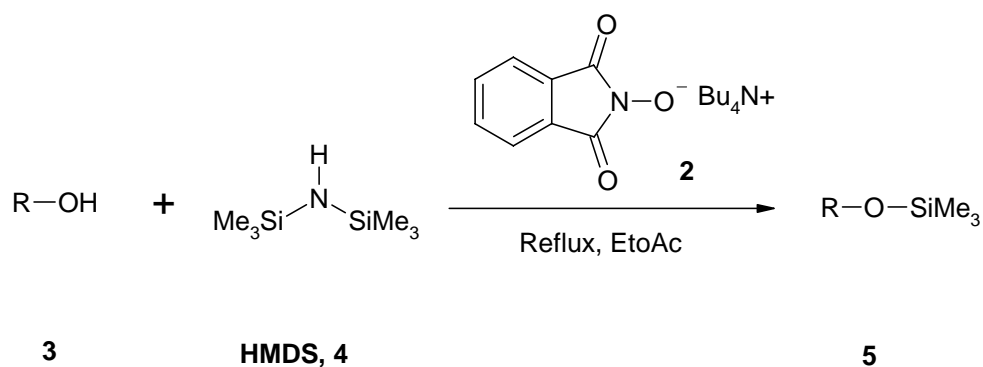
Result and discussion

TBAPINO (**2**) was prepared by addition of an equivalent of N-hydroxyphthalimide (NHPI, **1**) to an aqueous solution of tetrabutylammonium hydroxide at room temperature (**Scheme 1**). TBAPINO, as a novel organocatalyst, has good lifetime and was resistant to moisture and air. It could be used for months without loss of performance.



Scheme 1.

In the next stage, the catalytic applicability of TBAPINO was examined in the activation of HMDS (**4**) for the protection of 4-chlorobenzyl alcohol (**3b**) in different solvents at reflux or solvent-free conditions as a model reaction (**Scheme 2**).

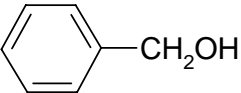
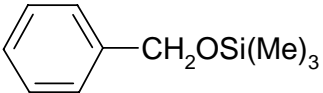
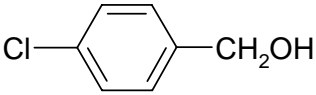
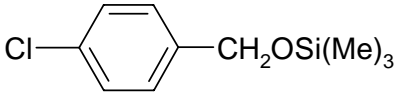
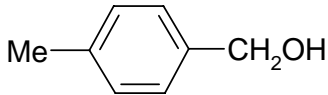
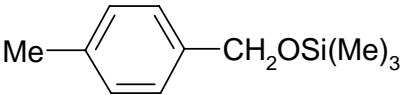
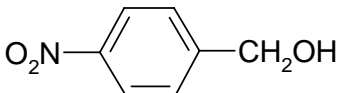
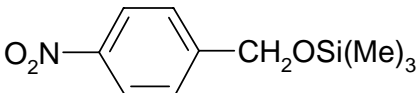
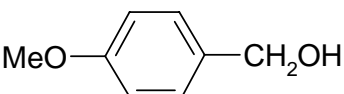
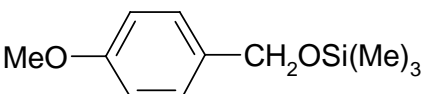
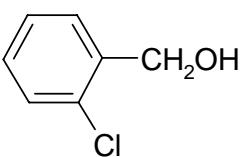
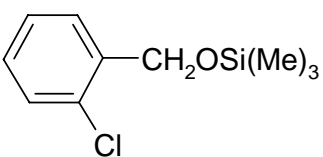
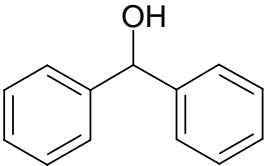
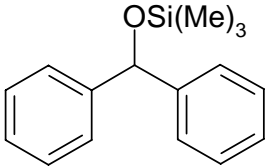


Scheme 2.

The effect of different solvents was studied on the efficiency of the model reaction. The obtained results showed that the efficiency and yields of reaction in EtOAc is more than that

observed in other solvents or even under neat conditions (Table 1, entry 2). Reaction of 4-chlorobenzyl alcohol and HMDS in the presence of 2 mol% of TBPAINO was completed after 20 min in EtOAc at reflux conditions.; therefore, these conditions were applied to the trimethylsilylation of other hydroxyl groups.

Table 1. TBAPINO-catalyzed silylation of alcohols using HMDS at optimized conditions

Entry	Substrate (3)	Product (5)	Time (Min.)	Isolated Yield (%)
1			20	98
2			30	97
3			15	98
4			75	94
5			15	96
6			25	97
7			45	95
8	CH ₃ CH ₂ OH	CH ₃ CH ₂ OSi(Me) ₃	60	96

The protection of a diverse alcohols such as primary, and secondary hindered alcohols was proceeded efficiently in high yields. Table 1 summarizes the results for TMS protection of various alcohols with HMDS in the presence of TBAPINO as catalyst.

In conclusion, Mildness of the reaction conditions, simple preparation of the organocatalyst, high efficiency, reasonable yields of products and clean work-up are among the outstanding advantages of this new method.

Experimental Section

To a mixture of alcohol (1.0 mmol) and HMDS (0.55 mmol) was added TBAPINO (2.0 mol%) and the mixture was stirred at reflux conditions for an appropriate length of time as appeared in Table 1. The reaction mixture was extracted twice by 3-5 mL portions of ethyl acetate (EtOAc) after TLC and GC monitoring showed completion of the reaction. The organic phases were washed by water and dried over anhydrous Na₂SO₄. The pure product was obtained after evaporation of the solvent.

Acknowledgment

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References

1. G. Sartori, R. Ballini, F. Bigi, G. Bosica, R. Maggi, P. Righi, *Chem. Rev.* **2004**, *104*, 199.
2. P. J. Wan, M. K. Dowd, A. E. Thomas, B. H. Butler, *J. Am. Oil Chem. Soc.* **2007**, *84*, 701.
3. J. Kusmierz, J. J. De George, D. Sweeney, D. May, S. I. Rapoport, *J. Chromatogr.* **1989**, *497*, 39.
4. T. W. Green, P. G.M. Wuts, *Protective Groups in Organic Synthesis*. Wiley: New York, **1999**.

5. W. C. Still, M. J. Schneider, *J. Am. Chem. Soc.* **1977**, *99*, 948.
6. M. Lalonde, T. H. Chan, *Synthesis* **1985**, 817.
7. M. A. Brook, *Silicon in Organic, Organometallics and Polymer Chemistry*. Wiley: New York, **2000**.
8. B. Karimi, B. Golshani, *J. Org. Chem.* **2000**, *65*, 7228.
9. J. Cossy, P. Pale, *Tetrahedron Lett.* **1987**, *28*, 6039.
10. W. Mormann, J. Demeter, *Macromolecules* **1999**, *32*, 1706.
11. Z. H. Zhang, T. S. Li, F. Yang, C. G. Fu, *Synth. Commun.* **1998**, *28*, 3105.
12. M. M. Mojtahedi, M. S. Abaee, V. Hamidi, A. Zolfaghari, *Ultrason. Sonochem.* **2007**, *14*, 596.
13. M. M. Mojtahedi, H. Abbasi, M. S. Abaee, *J. Mol. Catal. A: Chem.* **2006**, *250*, 6.
14. H. Firouzabadi, N. Iranpoor, S. Sobhani, S. Ghassamipour, *Synthesis* **2005**, 595.
15. N. Azizi, M. R. Saidi, *Organometallics* **2004**, *23*, 1457.
16. B. Akhlaghinia, S. Tavakoli, *Synthesis* **2005**, 1775.
17. A. V. Narsaiah, *J. Organomet. Chem.* **2007**, *692*, 3614.
18. V.H. Jadhav, K. S. A. Kumar, V. D. Chaudhari, D. D. Dhavale, *Synth. Commun.* **2007**, *37*, 1363.