Tetrabutylammonium Phthalimide-N-oxyl: An Efficient Organocatalyst for Trimethylsilylation of Alcohols and Phenols with Hexamethyldisilazane

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Tetrabutylammonium phthalimide-N-oxyl (TBAPINO) was found to be an effective organocatalyst for rapid, simple and chemoselective protection of the hydroxyl group of alcohols and phenols using hexamethyldisilazane (HMDS) under mild conditions. The low catalyst loading, high to quantitative yields and simple removal of the catalyst from the reaction mixture illustrate the other attractive features of this protocol.

Keywords: Trimethylsilylation, Alcohols, Phenols, Hexamethyldisilazane, Tetrabutylammonium phthalimide-N-oxyl, Organocatalysis

INTRODUCTION

At the dawn of the 21st century, organic chemistry witnessed a revolution in catalysis using small organic compounds-Organocatalysis. Nowadays, organocatalytic protocols are extensively pursued to replace the traditional catalytic approaches based on the use of toxic or precious transition-metals for the synthesis of organic compounds. Organocatalysts have several significant advantages over traditional metal catalysis. They are usually robust, inexpensive, readily available and non-toxic. Many organocatalysts are inert towards moisture and oxygen. Because of these unique features, no reaction conditions such as inert atmosphere, absolute solvents, etc. are to be observed in many instances. Furthermore, due to the absence of transition metals, organocatalytic methods seem to be especially attractive for the preparation of compounds that do not tolerate metal contamination, especially pharmaceuticals.

Thus, organocatalysts are making a valuable contribution to green chemistry [1,2]. Protection of hydroxyl groups is a common practice in synthetic organic and analytical chemistry. Various protecting methods such as tetrahydropyranylation, esterification, esterification and trialkylsilylation have been used for this purpose [3,4]. Among these methods, trimethylsilylation of hydroxyl group has received a lot of attention due to thermal stability, solubility in non-polar solvents, and enhanced stability of the resulting trimethylsilyl (TMS) ether derivatives under a variety of conditions. Furthermore, the removal of the protecting group can be easily accomplished by acid- or base-induced hydrolysis [3,5]. Trimethylsilylation is also extensively used for the derivatization of hydroxyl compounds to increase their volatility for gas chromatography and mass spectrometry [6]. Hence, different silylating agents such as chlorotrimethylsilane [7-9], trimethylsilyl triflate [10], hexamethyldisilane [11] and hexamethyldisiloxane have been used in the presence of a broad range of catalysts and reagents for the introduction of TMS group into a variety of alcohols or...