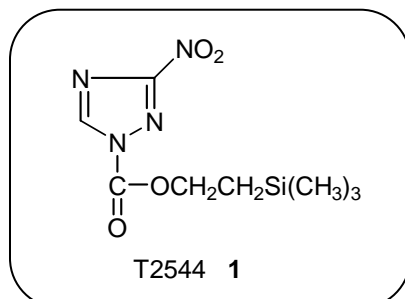
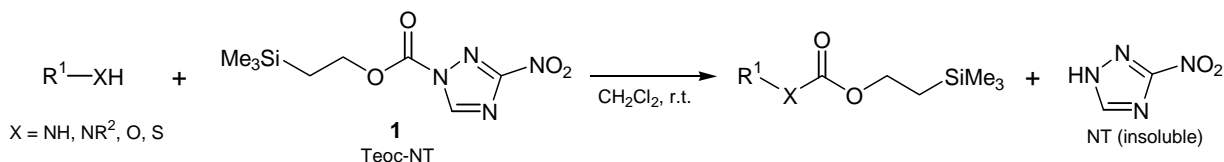


A Useful Protecting Reagent



Carbamates, carbonates, and thiocarbonates have been known for some time as versatile protecting groups for amines, alcohols, and thiols. Although alkyl chloroformates are the most frequently used reagents for the preparation of these protecting groups, they are hazardous liquids and are susceptible to thermolysis and hydrolysis, requiring careful handling and storage. Furthermore, the protection procedure normally requires the addition of base and long reaction times for complete coverage. Thus development of more practical and convenient protecting reagents is desirable.

Recently, Sodeoka and Shimizu have developed a useful reagent for the transformation, Teoc-NT (**1**) which is stable and easy to handle. They reported that **1** reacts rapidly with various amines, alcohols, and thiols at room temperature to give the corresponding protected compounds in high yields, respectively.



Entry	R ¹ -XH	1 (eq.)	additive	time	Y. (%)	Entry	R ¹ -XH	1 (eq.)	additive	time	Y. (%)
1		1	—	5 min	quant.	5		2	Et ₃ N (5 eq.)	60 min	94
2 ^a		1	—	5 min	95	6		4	Et ₃ N (10 eq.)	4 h	80
3 ^a		1	—	5 min	96	7 ^b		1	Et ₃ N (2 eq.)	5 min	92
4		1	—	30 min	quant.						

^a in CH₂Cl₂ / 5% NaHCO₃ (1 : 1)

The biphasic system was also effective, and the reaction was completed within 5 min.

Simple phase separation and evaporation afforded highly pure (>99%) carbamates

^b yield after washing with 5% NaHCO₃

Keywords : protecting reagent, Teoc-NT

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Head Office: TOKYO CHEMICAL INDUSTRY CO., LTD. Tel: +81-3-5640-8878 Fax: +81-3-5640-8902 E-mail: globalbusiness@tokyokasei.co.jp www.tci-asiapacific.com

For example, **1** reacts rapidly with a stoichiometric amount of amines in methylene chloride at room temperature to give corresponding protected compounds almost quantitatively. The by-product nitrotriazole (NT) has low solubility in the reaction solvent and precipitates out as a crystalline solid. As a result, NT can be removed by simple filtration and highly pure products can be obtained easily in many cases. Removal of trace amounts of NT in the reaction mixture can be readily effected by washing with 5% NaHCO₃ obviating the need for column chromatographic purification. In Entries 2-3, the reaction proceeded rapidly to completion using a biphasic system (CH₂Cl₂ / 5%NaHCO₃ (1:1)). Subsequent separation of the phases and removal of solvents *in vacuo* afforded highly pure products. In the case of primary amino alcohols, although longer reaction times were required, selective protection of the amino group was observed without formation of the carbonate or the cyclic carbamate (Entry 4). In the case of aromatic amines, which are less reactive than the associated aliphatic amines, addition of triethylamine as a base was required for the preparation of the desired protected compounds in high yields (Entry 5).

Introduction of the Teoc group at 2-NH₂ of guanosine derivatives, a reaction hitherto undocumented, also proceeded rapidly with the addition of triethylamine to give corresponding protected compounds in high yields (Entry 6). The Teoc group can be removed easily by the action of fluoride ions in neutral condition, rendering **1** applicable to the synthesis of various base-sensitive oligonucleotide derivatives.

Furthermore, the reaction of **1** with alcohols and thiols also proceeds rapidly in the presence of triethylamine to give corresponding *O*-Teoc compounds in high yields (Entry 7).

Thus, **1** is a useful protecting reagent which reacts rapidly with amines, alcohols, and thiols to give the respective carbamates, carbonates, and thiocarbonates with a simple and convenient procedure under mild conditions

T2544 2-(Trimethylsilyl)ethyl 3-nitro-1*H*-1,2,4-triazole-1-carboxylate

1g

Reference

M. Shimizu, M. Sodeoka, *Org. Lett.*, **2007**, *9*, 5231.

This product received license of invention of RIKEN



(Jpn Patent Appl., 2007-260255).