

## **Tetrabutylammonium Bromide: Effective Promoter Both In Silylation and Alkene Formation Via Dehydration of Alcohols**

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### **ABSTRACT**

*A mild and efficient method for the silylation of alcohols promoted by tetrabutylammonium bromide is reported. An interesting and unusual formation of alkene is observed in case of trimethylsilyl protection of secondary benzylic alcohols containing alkyl ethereal groups.*

**Keywords:** Alcohols, Trialkylsilylation, Tetrabutylammonium bromide, Dehydration, Alkenylation.

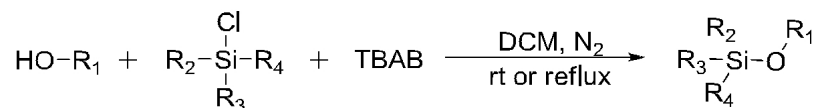
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### **INTRODUCTION**

Protection of alcohols is of high importance in multi-step synthesis and has attracted considerable attention of many organic chemists [1]. For this purpose the method for conversion of alcohols to their corresponding silyl ethers using trialkylsilyl chloride has been widely used, as trialkylsilyl chlorides are cheap and commercially available [2,3] among the various reagents that are available for the silylation of alcohols [4-6]. Recently Pizzo *et. al.* [7], have reported their work on the trimethyl silylation of alcohols accelerated by tetrabutylammonium bromide using trimethylsilyl azide as a silylating agent. More recently Shirini *et. al.*, [8] also have reported the trimethylsilylation of primary and secondary alcohols with hexamethyldisilazane (HMDS) catalyzed by tetrabutylammonium bromide. However, these reports were limited to only trimethyl silylation of alcohols using expensive and toxic silylating agents. Likewise, most of reports on silylation of alcohols suffer some serious drawbacks like need of long reaction time, drastic reaction conditions, or tedious work-up procedures. On account of these drawbacks, we herein wish to report the application of tetrabutylammonium bromide on promoting the

silylating ability of trialkylsilyl chloride. The protocol is mild and can efficiently silylate the alcohols by using trialkylsilyl chloride in the presence of tetrabutylammonium bromide (Scheme 1).

**Scheme 1**



## MATERIALS AND METHODS

All chemicals were purchased from *Sigma-Aldrich* or *S.D. Fine Chemicals Pvt. Ltd., India* and used as received. *ACME* silica gel (100–200 mesh) was used for column chromatography and reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm silica gel coated glass plates 60F254 using UV light as visualizing agent and iodine or *p*-anisaldehyde solution followed by heating as developing agent. All the other chemicals and solvents were obtained from commercial sources and purified using standard methods. All the trialkylsilyl ethers are known compounds and characterised by NMR and MS, and the obtained spectroscopic results are in agreement with the literature data.

### General Procedure

**For silylation of alcohol:** Tetrabutylammonium bromide (1.0 mmol) was added to a stirred solution of alcohol (1.0 mmol) and silylating agent (1.2 mmol) in DCM (3 mL) at room temperature or reflux at 40°C in N<sub>2</sub> atmosphere. The reaction was monitored by TLC. After completion of the reaction, the solvent was evaporated under reduced pressure. Ethyl acetate was added to the residue, washed with water (3X10 mL) and then the organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The crude product was loaded on a silica gel column and eluted with hexane and acetone as eluting mixture to afford the pure product.

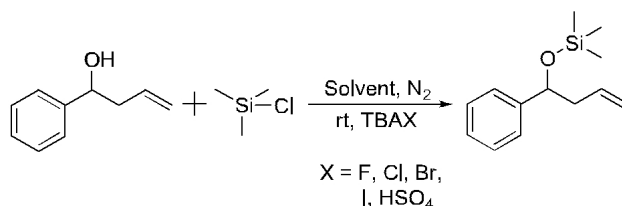
**For alkene synthesis:** Tetrabutylammonium bromide (1.0 mmol) was added to a stirred solution of alcohol (1.0 mmol) and trimethylsilylchloride agent (1.2 mmol) in toluene (3 mL) at 110 °C in N<sub>2</sub> atmosphere. The reaction was monitored by TLC. After completion of the reaction, the solvent was evaporated under reduced pressure. Ethyl acetate was added to the residue, washed with water (3X10 mL) and then the organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The crude product was loaded on a silica gel column and eluted with hexane and acetone as eluting mixture to afford the pure product.

## RESULTS AND DISCUSSION

Initially, we examined the reaction between 1-phenylbut-3-en-1-ol and trimethylsilyl chloride as model substrates using various solvents and tetrabutylammonium salts to obtain the desired product trimethyl (1-phenylbut-3-enyloxy) silane (Table1). To examine the promoting ability of various commercial available tetrabutylammonium salts, the reaction was carried out with model substrates using dichloromethane as solvent and it was found that tetrabutylammonium bromide is the best for the silylation of alcohols (Table 1, Entry 3). Furthermore, the reactions were performed using various solvents and as seen from Table 1, solvents like DCM, DCE, toluene and DMF (Table 1, Entry 3, 6, 7 and 8) provide much superior results compared to other solvents which were either giving low or no yield of the desired product (Table 1, Entry 9 to 15).

Moreover, we have also found that reaction without TBAB was very sluggish and in some cases not even initiated, which apparently indicates the role of tetrabutylammonium bromide as promoter for these reactions.

**Table 1 Optimization of reaction conditions with model substrates 1-phenylbut-3-en-1-ol and trimethylsilyl chloride as model substrates using various solvents and tetrabutylammonium salts<sup>a</sup>**



S. No.	Solvent	TBAX	Time (h)	Yield (%) <sup>b</sup>
1.	DCM	TBAF	4	0
2.	DCM	TBACl	4	15
3.	DCM	TBABr	4	98
4.	DCM	TBAI	4	60
5.	DCM	TBAHSO <sub>4</sub>	4	22
6.	DCE	TBABr	4	90
7.	Toluene	TBABr	4	88
8.	DMF	TBABr	4	60
9.	DMSO	TBABr	4	0
10.	THF	TBABr	4	0
11.	Acetone	TBABr	4	0
12.	acetonitrile	TBABr	4	0
13.	PEG 400	TBABr	4	0
14.	H <sub>2</sub> O	TBABr	4	0
15.	DCM	-	4	10 <sup>c</sup>

<sup>a</sup> Reaction condition: Alcohol (1.0 mmol), TBAX (0.6 mmol), Trimethylsilyl chloride (1.2 mmol) and 5 ml of solvent in N<sub>2</sub> atmosphere at room temperature.

<sup>b</sup> Isolated yield.

<sup>c</sup> Reaction were performed without any promoter.

After optimizing reaction under various conditions the best reaction condition was found to be 1.0 mmol of alcohol, 0.6 mmol tetrabutylammonium bromide and 1.2 mmol of trialkylsilyl chloride in 5 ml dichloromethane. A wide range of structurally diverse alcohols are subjected to these optimized condition and tabulated in Table 2. As seen from Table 2, primary and secondary alcohols afforded excellent conversion to the corresponding silyl ethers (Table 2, Entry 1 to 24) at room temperature. However, in case of tertiary or hindered alcohols, it is required to either reflux or stir the reaction mixture for longer time or both (Table 2, Entry 25).

**Table 2. Silylation of various alcohol under optimized reaction condition**

S. No.	Alcohol	Product	Time (h)	Yield (%) <sup>b</sup>
1.	PhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	PhCH(OTMS)CH <sub>2</sub> CHCH <sub>2</sub>	4	98
2.	PhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	PhCH(OTBDMS)CH <sub>2</sub> CHCH <sub>2</sub>	2	97
3.	PhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	PhCH(OTIPS)CH <sub>2</sub> CHCH <sub>2</sub>	2	97
4.	PhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	PhCH(OTES)CH <sub>2</sub> CHCH <sub>2</sub>	3	99
5.	<i>p</i> -MePhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>p</i> -MePhCH(OTMS)CH <sub>2</sub> CHCH <sub>2</sub>	2	98
6.	<i>p</i> -MePhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>p</i> -MePhCH(OTBDMS)CH <sub>2</sub> CHCH <sub>2</sub>	2	97
7.	<i>p</i> -BrPhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>p</i> -BrPhCH(OTMS)CH <sub>2</sub> CHCH <sub>2</sub>	5	88
8.	<i>p</i> -BrPhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>p</i> -BrPhCH(OTBDMS)CH <sub>2</sub> CHCH <sub>2</sub>	4	90
9.	<i>p</i> -OHPhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>p</i> -OHPhCH(OTMS)CH <sub>2</sub> CHCH <sub>2</sub>	3	92
10.	<i>p</i> -OHPhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>p</i> -OHPhCH(OTBDMS)CH <sub>2</sub> CHCH <sub>2</sub>	2	95
11.	<i>m</i> -NO <sub>2</sub> PhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>m</i> -NO <sub>2</sub> PhCH(OTMS)CH <sub>2</sub> CHCH <sub>2</sub>	5	87
12.	<i>m</i> -NO <sub>2</sub> PhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>m</i> -NO <sub>2</sub> PhCH(OTBDMS)CH <sub>2</sub> CHCH <sub>2</sub>	4	90
13.	PhCH(OH)CH <sub>3</sub>	PhCH(OTMS)CH <sub>3</sub>	2	95
14.	PhCH(OH)CH <sub>3</sub>	PhCH(OTBDMS)CH <sub>3</sub>	1	99
15.	PhCH(OH)CH <sub>3</sub>	PhCH(OTIPS)CH <sub>3</sub>	2	96
16.	<i>p</i> -BrPhCH(OH)CH <sub>3</sub>	<i>p</i> -BrPhCH(OTMS)CH <sub>3</sub>	3	89
17.	<i>p</i> -BrPhCH(OH)CH <sub>3</sub>	<i>p</i> -BrPhCH(OTBDMS)CH <sub>3</sub>	2	91
18.	PhCH <sub>2</sub> OH	PhCH <sub>2</sub> OTMS	1	92
19.	PhCH <sub>2</sub> OH	PhCH <sub>2</sub> OTBDMS	1	95
20.	PhOH	PhOTMS	1	88
21.	PhOH	PhOTBDMS	1	90
22.	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> CH <sub>2</sub> OH	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> CH <sub>2</sub> OTMS	3	91
23.	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> CH <sub>2</sub> OH	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> CH <sub>2</sub> OTBDMS	3	95
24.	PhCH <sub>2</sub> CH(OH)CH <sub>3</sub>	PhCH <sub>2</sub> CH(OTMS)CH <sub>3</sub>	5	85
25.	Ph <sub>3</sub> COH	Ph <sub>3</sub> COTMS	6	81 <sup>c</sup>

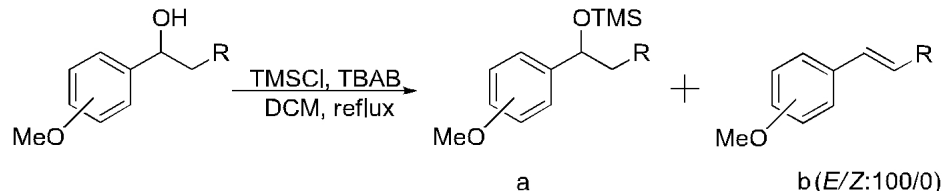
<sup>a</sup>Reaction condition: Alcohol (1.0 mmol), TBAB (0.6 mmol), Trialkylsilyl chloride (1.2 mmol) and 5 ml DCM in N<sub>2</sub> atmosphere.

<sup>b</sup> Isolated yield.

<sup>c</sup> Reaction were performed in refluxing DCM (40 °C).

Under the optimized reaction conditions, when secondary benzylic alcohols containing alkyl ethereal groups were used, the reaction afforded two products. The first one is due to the dehydrative cleavage of carbon-oxygen bond that results in the formation of the corresponding alkene and the other from the silylation of alcohol (Table 3). To the best of our knowledge formation of alkene under these conditions has been not reported so far.

**Table 3. Trimethylsilylation of secondary benzyl alcohol containing alkyl ether group.<sup>a</sup>**



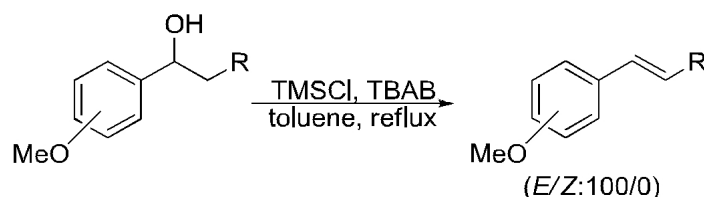
S. No.	Alcohol	Time (h)	Yield(a/b)(%) <sup>b</sup>
1.	<i>p</i> -MeOPhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	4	40/60
2.	<i>p</i> -MeOPhCH(OH)CH <sub>3</sub>	2	42/58
3.	3,4,5-MeOPhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	2	45/55

<sup>a</sup>Reaction condition: Alcohol (1.0 mmol), TBAB (0.6 mmol), Trimethylsilyl chloride (1.2 mmol) and 5 ml DCM in N<sub>2</sub> atmosphere.

<sup>b</sup> Isolated yield.

As can be seen from Table 3, trimethylsilylation of alkylether substituted secondary benzylic alcohol favour the formation of alkenylated product over silylation of alcohol (Table 3, Entry 1 to 3). Encouraged by these results, we further optimized the reaction condition so as to obtain good yields of alkenes and the best condition was found to be when the reaction was performed under refluxing toluene. Table 4 shows the scope of the reaction for alkene synthesis and as can be seen all the alkyl ether containing substrates when subjected to the optimized reaction conditions under reflux in toluene providing excellent yield of the alkenylated products ( Table 4, Entry 1 to 3).

**Table 4. Alkenylation of secondary benzyl alcohol containing alkyl ether group under optimized reaction condition.<sup>a</sup>**



S. No.	Alcohol	Product	Time (h)	Yield(%) <sup>b</sup>
1.	<i>p</i> -MeOPhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	<i>p</i> -MeOPhCHCHCHCH <sub>2</sub>	4	100
2.	<i>p</i> -MeOPhCH(OH)CH <sub>3</sub>	<i>p</i> -MeOPhCHCH <sub>2</sub>	4	100
3.	3,4,5-MeOPhCH(OH)CH <sub>2</sub> CHCH <sub>2</sub>	3,4,5-MeOPhCHCHCHCH <sub>2</sub>	4	100

<sup>a</sup> Reaction condition: Alcohol (1.0 mmol), TBAB (0.6 mmol), Trimethylsilyl chloride (1.2 mmol) and 5 ml Toluene in N<sub>2</sub> atmosphere.

<sup>b</sup> Isolated yield.

The mechanism of the reaction is not clear, however there are reports which clearly shown the role of tetrabutylammonium bromide as a promoter [7,8]. We are on course for further investigating on this reaction for a clear mechanistic view.

## APPLICATIONS

The Protection of alcohols is of high importance in multi-step synthesis and attracted considerable attention of many organic chemists. A mild and efficient method for silylation of alcohols promoted by tetrabutylammonium bromide is reported. An interesting and usual formation of alkenes is observed in case trimethyl silyl protection of secondary benzylic alcohols containing alkyl ethereal groups.

## CONCLUSION

In conclusion, we have demonstrated that tetrabutylammonium bromide is an efficient promoter for the silylation of alcohols using various trialkylsilyl chloride under mild reaction conditions and in alkene formation in case of trimethylsilyl protection of secondary benzylic alcohols containing alkyl ethereal groups. High yields of the products, relatively short reaction times, simple and easy work-up procedure can be considered as the main advantages of the reported methods.

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**REFERENCES**

- [1] a) L.F. Fieser, M. Fieser, Reagents for Organic Synthesis, John Wiley and Sons Inc., New York, 1999; b) C.B. Reese, Protective Groups in Organic Chemistry, ed by J. F. McOmien, Plenum Press, London, **1973**.
- [2] S. Tarkelson, C. Ainsworth, *Synthesis* **1976**, 722.
- [3] J. Cossy, P. Pale, *Tetrahedron Lett.* **1987**, 28, 6039.
- [4] J.M. Aizpurua, C. Palomo, *Bull. Soc. Chim. Fr. Mem.* **1982**, 265.
- [5] I. Nishiguchi, Y. Kita, M. Watanabe, Y. Ishino, T. Ohno and H. Maekawa, *Synlett* **2000**, 1025.
- [6] W. Verboom, G.W. Visser and D.N. Reinhoudt, *Synthesis* **1981**, 807.
- [7] D. Amantini, F. Fringuelli, F. Pizzo and L. Vaccaro, *J. Org. Chem.* **2001**, 66, 6734.
- [8] F. Shirini and M. Abedini *J. Iran. Chem. Soc.* **2008**, 5, Suppl. S87-S90.