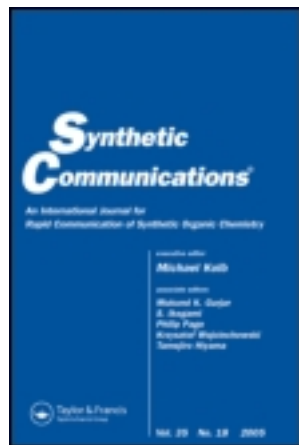


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A Convenient Method for Protection and Deprotection of Alcohols and Phenols as Alkylsilyl Ethers Catalyzed by Iodine Under Microwave Irradiation

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A Convenient Method for Protection and Deprotection of Alcohols and Phenols as Alkylsilyl Ethers Catalyzed by Iodine Under Microwave Irradiation

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ABSTRACT

Irradiation of alcohols or phenols with *tert*-butyldimethylsilyl chloride (TBDMSCl) or trimethylsilyl chloride (TMSCl) in presence

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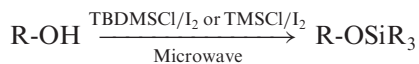


of catalytic amount (20 mol%) of iodine in a microwave oven for 2 min gives the corresponding silyl ethers in excellent yield. Iodine in methanol deprotects the silyl ether into its parent alcohol or phenol under similar reaction conditions.

Key Words: *O*-Silylation; TBDMS ether; TMS ether; Iodine catalyzed; Microwave irradiation.

O-Silylation of alcohols was mainly a derivatization process to increase the volatility and stability of polar organic compounds in gas chromatographic analysis.^[1] But after early 70's, the potential of silyl group as a hydroxyl group protecting agent was acknowledged and gradually it became the most widely used alcohol protecting group.^[2] *tert*-Butyldimethylsilyl (TBDMS) as well as trimethylsilyl (TMS) protecting groups are seen to have wide application in synthetic sequences of organic molecules, especially natural products like prostaglandin,^[3] steroid,^[4] carbohydrate etc.^[5] In addition to its use as a hydroxyl protecting group, the silyl group has the ability to control stereoselectivity in many reactions.^[6] The most common method of silylation of alcohol is the reaction with trialkylsilyl chloride and a suitable base.^[2]

Few other important reagents described for the preparation of TMS ether are HMDS with TMSCl,^[7] *N,O*-bis(trimethylsilyl)acetamide,^[8] 1-(trimethylsilyl)imidazole,^[9] TMSCl-Li₂S,^[10] or Mg.^[11] Upadhyay et al.^[12] had reported natural kaolinite clay as a catalyst for *O*-trimethylsilylation reaction while Karimi and Golshani^[13] reported iodine as a catalyst with HMDS.



Recently Amantini et al.^[14] had reported a method of *O*-trimethylsilylation of alcohol and phenol using trimethylsilylazide catalyzed by tetrabutylammonium bromide under solvent free condition. But there is no corresponding reagent for *tert*-butyldimethylsilyl ether formation. For the preparation of the *tert*-butyldimethylsilyl ether of alcohol the most commonly used reagent is the TBDMSCl with imidazole in DMF.^[15] For tertiary and hindered secondary alcohols *tert*-butyldimethylsilyl triflate with 2,6-lutidine as base is used.^[16] Few other reagents for this conversion are TBDMSCl with Li₂S,^[10] TBDMSCl with DMAP and trimethylamine,^[17] allyl-*tert*-butyldimethylsilane with *p*-toluenesulfonic acid^[18] etc.

Herein, we wish to report a new commercially available cheap catalyst for silylation of alcohol and phenol with TBDMSCl or

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TMSCl. During the course of our endeavour for development of environment friendly synthetic methods, utilization of microwave dielectric heating effect has been studied in few reactions with iodine as a catalyst. Use of microwave irradiation in organic reactions is advantageous in many ways because of short reaction time, cleaner reaction products, and solvent free reaction conditions.^[19] Although different hypotheses have been put forwarded to account for the effect of microwave on organic reactions/compounds^[20] the reason for the dramatic acceleration effect is thought to be instantaneous super heating of the reaction medium. Regardless of the exact origin of the microwave effect, it is found to be extremely efficient and applicable to a very broad range of practical syntheses including combinatorial one.^[21] In this laboratory also reactions like acetalization,^[22] enol-acetylation,^[23] DHP ether formation,^[24] etc., were performed under microwave irradiation.^[25] Continuing the same effort when an alcohol in 1,2-dichloroethane was irradiated with TMSCl in a microwave oven at 90 W power or with TBDMSCl at 360 W power and catalytic amount (20 mol%) of iodine for about 2 min the corresponding silyl ether was formed in excellent yield. Primary, secondary, and tertiary as well as allylic, benzylic, and phenolic hydroxyl groups were easily transformed into the corresponding silyl ethers. The results are presented in Table 1.

From the Table 1, it is clear that the reaction is high yielding with yields ranging from 91 to 96% within a short period of time. Although the existing methods for TMS ether formation gives similar yields, most of these methods take several hours for completion at r.t. In case of TBDMS ether the present method has the advantage of short reaction time and high yield. The reagent is equally suitable for primary, secondary, tertiary as well as allylic, benzylic, and phenolic hydroxyl groups. When 1.5 M equiv. of TBDMSCl is used the yield of the corresponding silyl ether is around 60 to 68% with recovery of the unreacted starting material during purification. If we consider the yield based on reacted starting material (BRSM) the actual yield turns out to be more than 90%. When the molar equivalent of TBDMSCl added is increased to 2.5 equiv., the yield of the TBDMS ether increased to around 95%.

Most of the time it is observed that a catalyst used for protection of a functional group can also act as a deprotecting reagent if used alone under some harsher conditions. In case of trimethylsilyl ether and *tert*-butyldimethylsilyl ether, deprotection is generally done with a mild acidic solution or with a fluoride ion.^[2] We have also observed like Vaino and Szarek^[28] that iodine acts as a deprotecting reagent for conversion of TMS ether and TBDMS ether into their parent alcohol under microwave irradiation in methanol at 360 and 640 W of power respectively. All the



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Table 1. Formation of silyl ethers with TMSCl–iodine and TBDMSCl–iodine.^a

Substrate	Yield % at 90 W with TMSCl 1.3 M equiv.	Yield % at 360 W with TBDMSCl 1.5 M equiv. (BRSM)	Yield % at 2.5 M equiv.	Ref.
Hexadecanol	96	68 (93)	94	[26a]
1-Docosanol	92	65 (96)	95	[26b]
2,2,2-Trichloroethanol	92	63 (93)	92	[26c]
Cyclohexanol	93	62 (97)	95	[10]
Cholesterol	94	62 (92)	93	[17]
1-Menthol	94	68 (95)	95	[12]
Borneol	93	67 (93)	94	[14]
<i>t</i> -Butanol	90	67	92	[12]
Terpeneol	91	66	94	[26d]
Linalool	92	67 (91)	92	[14]
Benzyl alcohol	95	65 (95)	94	[10]
<i>p</i> -Anisyl alcohol	94	66 (94)	95	[27]
1-Phenylethanol	94	68 (93)	94	[27]
Allyl alcohol	94	63	95	[12]
Cinnamyl alcohol	93	68 (87)	93	[14]
Phenol	95	64 (94)	94	[10]
<i>O</i> -Cresol	94	65 (93)	94	[26e]

^aThe products were characterized by spectral (IR, NMR, MS) analysis as well as comparison with authentic materials prepared by known methods.

silyl ethers reported in Table 1 were deprotected by iodine to the corresponding alcohols in quantitative yield.

EXPERIMENTAL SECTION

General Procedure for Silylation of Hydroxyl Groups

To a solution of 2 mmol of an alcohol or phenol in 1.5 mL of 1,2-dichloroethane was added 2.6 mmol of TMSCl or 3 mmol of TBDMSCl (as the case may be) and 52 mg (0.2 mmol) of iodine. The solution was taken in a 50 mL conical flask and placed in a kitchen type microwave oven^[25] (LG brand, model MS-28MC “multiwave”). A small funnel was placed in the mouth of the flask to reduce possible loss of solvent by evaporation. The solution was irradiated at 90 W of power for TMS ether and 360 W of power for TBDMS ether for 120 s (Table 1). The tempera-

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ture of the reaction mixture was between 46 to 50°C for TMS ether and 71 to 72°C for TBDMS ether when recorded immediately after irradiation. The solution was diluted with dichloromethane, washed with a dilute solution of sodium thiosulfate followed by water and dried over anhydrous sodium sulfate. Evaporation of the solvent at reduced pressure yielded almost pure product. Purification through a short column was done when necessary.

General Procedure for Desilylation of Silyl Ethers

To a solution of 2 mmol of silyl ether in 1.5 mL of methanol was added 0.2 mmol of iodine and the solution was irradiated in a microwave oven for 130–180 s at a power setting of 360 W for TMS ether and 640 W for TBDMS ether as described in the previous experimental procedure. Work up in the similar way afforded a quantitative yield of the corresponding alcohol, which was confirmed by comparison with the authentic material.

ACKNOWLEDGMENT

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25. In its most widely used and simplest version such reactions are performed in domestic microwave ovens, although more sophisticated microwave reactors are now becoming available.



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26. NMR (60 MHz) peaks of the TBDMS ether at δ ppm are (a) 3.40 (t, $J=6$ Hz, 2H), 1.14 (m, 28H), 0.82 (s, 9H), 0.78 (t, $J=6$ Hz, 3H), 0.20 (s, 6H); (b) 3.38 (t, $J=6$ Hz, 2H), 1.13 (m, 40H), 0.80 (s, 9H), 0.76 (t, $J=6$ Hz, 3H), 0.20 (s, 6H); (c) 4.00 (br s, 2H), 0.90 (s, 9H), 0.30 (s, 6H); (d) 6.15 (m, 1H), 3.25 (m, 1H), 2.20 (m, 6H), 2.02 (s, 3H), 1.80 (s, 6H), 0.78 (s, 9H), 0.20 (s, 6H); (e) 6.30–7.00 (m, 4H), 1.90 (s, 3H), 0.70 (s, 9H), 0.10 (s, 6H).
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