

Direct Conversion of Trimethylsilyl and Tetrahydropyranyl Ethers into Their Bromides and Iodides Under Neutral Conditions Using *N*-Bromo and *N*-Iodosaccharins in the Presence of Triphenylphosphine

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Trimethylsilyl and tetrahydropyranyl ethers were easily converted into their corresponding bromides and iodides with high efficiency and selectivity by *N*-bromo- and *N*-iodosaccharins in the presence of triphenylphosphine under neutral conditions. The reaction of trimethyloctyloxysilane as a model compound was studied in different solvents with different ratios of silyl ethers, triphenylphosphine and *N*-halosaccharin at room temperature, in order to optimize the reaction conditions.

Keywords: Silyl and tetrahydropyranyl ethers, *N*-Bromosaccharin, *N*-Iodosaccharin, Triphenylphosphine, Bromide, Iodide

INTRODUCTION

Silyl and tetrahydropyranyl ethers are important precursors for the preparation of many other compounds and their preparation from hydroxyl groups has been under attention in recent years [1]. Due to the ease of preparation and purification of silyl and tetrahydropyranyl ethers and their sufficient chemical reactivity, their controlled transformation into other functional groups is of value in organic synthesis.

Direct conversion of protected alcohols into their corresponding halides is a useful synthetic transformation. Some of the developed methods for this purpose, include boron tribromides [2], triphenylphosphine dibromides [3], triphenylphosphine and carbontetrabromide [4], 2,4,4,6-tetra-bromo-2,5-cyclohexadienone [5], SiO₂-Cl/NaI [6], 1,2-bis(triphenylphosphino) ethane tetrahalide [7], and *N,N*-dimethylphosgeniminium chloride [8]. Development of new methods for this transformation is still of high demand and practical importance. Along this line, we have introduced

several reagent systems using Ph₃(SCN)₂ [9a], phosphine ionic liquid (IL-PPh₂) [9b] and 4-aminophenoxy diphenylphosphine [9c] for conversion of protected alcohols into other functionalities as well as into their halides.

Saccharin has been used as a sweetening agent in food and drug industries as a cheap and easily available compound. Halogenation of saccharin is easily achieved by to known procedures [10]. *N*-Halosaccharins (XNSac, X = Cl, Br, I) are stable crystalline compounds, soluble in most common organic solvents and insoluble in water [10a,11]. *N*-halosaccharins are more electrophilic than their analogues such as *N*-haloamides. *N*-halosaccharin is an oxidizing [12] and halogenating agent which is often employed for the halogenation of alkenes, activated aromatic compounds, enol acetates and 1,3-diones and *etc.* [11,13].

Recently, we have reported an efficient method for conversion of alcohols into their bromides or iodides using their corresponding *N*-halosaccharins in the presence of Ph₃P [14]. Herein we report that *N*-bromo- and *N*-iodosaccharins in the presence of triphenylphosphine can also be successfully applied as an efficient and selective system for one-pot

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conversion of structurally diverse silyl and tetrahydropyranyl ethers into their bromides and iodides with high efficiency and selectivity.

EXPERIMENTAL

Chemicals were purchased from Merck and Fluka Chemical Companies. The products were characterized by comparison of their physical data with those of known samples or by their spectral data. NMR spectra were recorded on a Bruker Avance DPX-250 spectrometer. The purity of the products and the progress of the reactions were accomplished by GC or TLC on silica gel polygram SILG/UV254 plates.

Typical Procedure for the Conversion of Benzyloxytrimethylsilane into its Bromide or Iodide in the Presence of XNSac/Ph₃P

To a flask containing a stirring mixture of XNSac (0.52 g, 2 mmol, X = Br or 0.63 g, 2 mmol, X = I) and Ph₃P (0.52 g, 2 mmol) in dry CH₂Cl₂ (25 ml), was added benzyloxytrimethylsilane (0.18 g, 1 mmol) at room temperature. The progress of the reaction was monitored by TLC or GC. After completion of the reaction, the solvent was evaporated. Column chromatography of the resulting crude mixture on silica-gel using *n*-hexane/ethyl acetate (1/5) afforded benzyl bromide in 95% isolated yield and the corresponding iodide in 90% isolated yield (Table 1, entry 1).

Typical Procedure for the Conversion of 2-Benzyloxytetrahydropyran into its Bromide or Iodide in the Presence of XNSac/Ph₃P

To a flask containing a stirring mixture of XNSac (0.65 g, 2.5 mmol, X = Br or 0.79 g, 2.5 mmol, X = I, 2.5 mmol, I) and Ph₃P (0.065 g, 2.5 mmol) in refluxing CH₃CN (25 ml), was added 2-benzyloxy tetrahydropyran (0.17 g, 1 mmol). Progress of the reaction was monitored by TLC and GC. After completion of the reaction, solvent was evaporated. Column chromatography on silica-gel of the crude mixture using *n*-hexane/ethyl acetate (10/1) gave the desired bromide in 80% isolated yield and the iodide in 79% isolated yield.

RESULTS AND DISCUSSION

In order to optimize the reaction conditions we studied the reaction of trimethyloctyloxysilane (Table 1, entry 7) as a model compound in different solvents with different ratios of silyl ethers, triphenylphosphine and *N*-halosaccharin at room temperature. We have found that when the reaction was proceeded in dichloromethane, a molar ratio of silyl ethers, triphenylphosphine, *N*-halosaccharin 1/2/2 was required to convert in high yield trimethyloctyloxysilane into its bromide or iodide. However, we applied similar reaction conditions for the conversion of primary, secondary alkyl, aryl and benzyl silyl ethers into their bromides and iodides. The reactions proceeded well and the desired bromides and iodides were isolated in excellent yields. The results of this study are summarized in Table 1.

We have also studied conversion of tetrahydropyranyl ethers into their corresponding bromides and iodides using triphenylphosphine and *N*-halosaccharins system. For this purpose, first we studied the conversion of 2-octyloxytetrahydropyran (Table 2, entry 7) as a model compound in order to optimize the reaction conditions with respect to the solvent and the molar ratio of triphenylphosphine/*N*-halosaccharins. We have found that the conversion of 1-octyloxytetrahydropyran (1 mmol) to its corresponding bromide (85% isolated) or iodide (80% isolated) requires 3 mmol of XNSac and PPh₃, respectively in refluxing CH₃CN. We applied similar reaction conditions for the conversion of structurally different tetrahydropyranyl ethers with success (Table 2). As it is clear from data presented in Tables (1 and 2), the method is more effective for the conversion of silyl ethers into their bromides and iodides than tetrahydropyranyl ones.

The most probable reaction mechanism is believed to proceed *via* the initial nucleophilic attack of triphenylphosphine to *N*-halosaccharin to afford the generation of phosphonium salt (**I**). Nucleophilic attack at the tetracoordinate phosphorous atom in (**I**) by silyl or tetrahydropyranyl ethers afforded (**II**) which is susceptible to nucleophilic attack by the halide anion to produce the desired halide plus triphenyl phosphine oxide (Scheme 1).

We have also studied the selectivity of the method in different binary mixtures by GC. The results of this study show that the method is highly selective and differentiates

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Table 1. Conversion of Silyl (TMS) Ethers to Alkyl Bromides and Iodides by XNSac/PPh₃

$$\text{ROSiMe}_3 \xrightarrow[\text{CH}_2\text{Cl}_2, \text{ r.t.}]{\text{XNSac / Ph}_3\text{P}} \text{RX}$$

X = Br, I

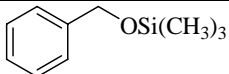
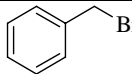
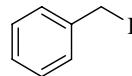
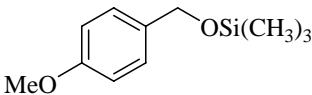
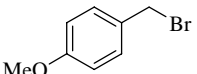
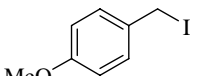
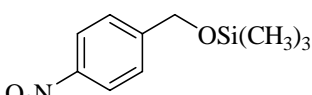
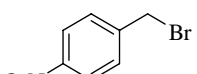
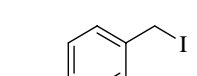
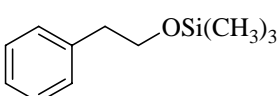
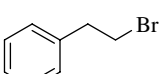
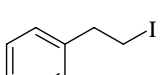
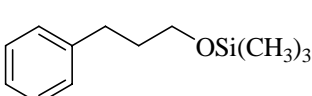
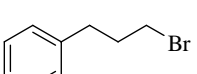
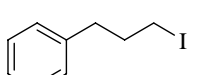
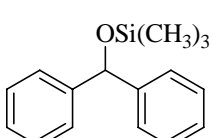
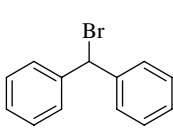
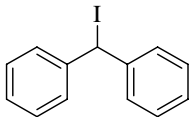
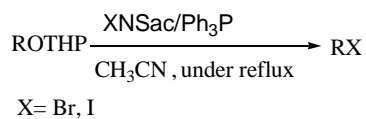
| Entry | Substrate | Product | Time (min) | Yield (%) ^a |
|-------|---|--|-------------|------------------------|
| 1 |  |  | Immediately | 95 |
| | |  | 10 | 90 |
| 2 |  |  | Immediately | 93 |
| | |  | 5 | 90 |
| 3 |  |  | 20 | 92 ^b |
| | |  | 35 | 90 ^b |
| 4 |  |  | 10 | 97 |
| | |  | 25 | 89 |
| 5 |  |  | 10 | 90 |
| | |  | 30 | 87 |
| 6 |  |  | 15 | 95 |
| | |  | 120 | 85 ^b |

Table 1. Continued

| | | | | |
|---|--|--|-----|----|
| 7 | | | 5 | 93 |
| | | | 40 | 91 |
| 8 | | | 20 | 94 |
| | | | 100 | 90 |

^aIsolated yields. ^b3 mmol of the reagent (BrNSac/Ph₃P) was used.

Table 2. Conversion of Tetrahydropyranyl (THP) Ethers to Alkyl Bromides and Iodides by NXSac/PPh₃

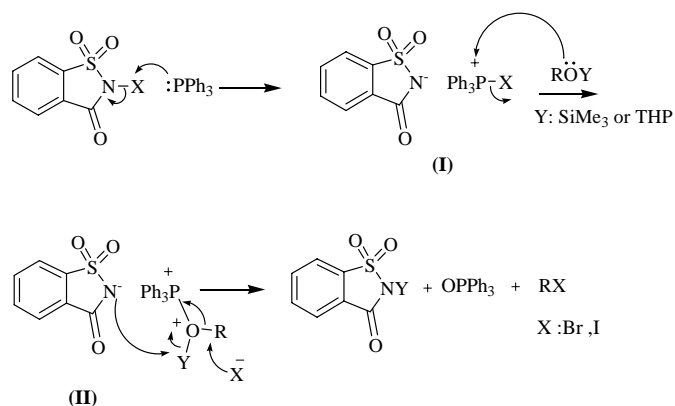
| Entry | Substrate | Product | Time (min) | Yield (%) ^a |
|-------|-----------|---------|------------|------------------------|
| 1 | | | 60 | 80 |
| | | | 70 | 79 |
| 2 | | | 20 | 90 |
| | | | 25 | 85 |
| 3 | | | 30 | 80 |
| | | | 40 | 75 |
| 4 | | | 40 | 73 |
| | | | 180 | 70 |

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Table 2. Continued

| | | | | |
|---|--|--|-----|-----------------|
| 5 | | | 80 | 75 |
| | | | 90 | 70 |
| 6 | | | 60 | 70 |
| | | | 120 | 80 ^b |
| 7 | | | 60 | 85 |
| | | | 240 | 80 |
| 8 | | | 120 | 82 |
| | | | 180 | 80 |

^aIsolated yields. ^b4 mmol of the reagent (BrNSac/Ph₃P) was used.



Scheme 1

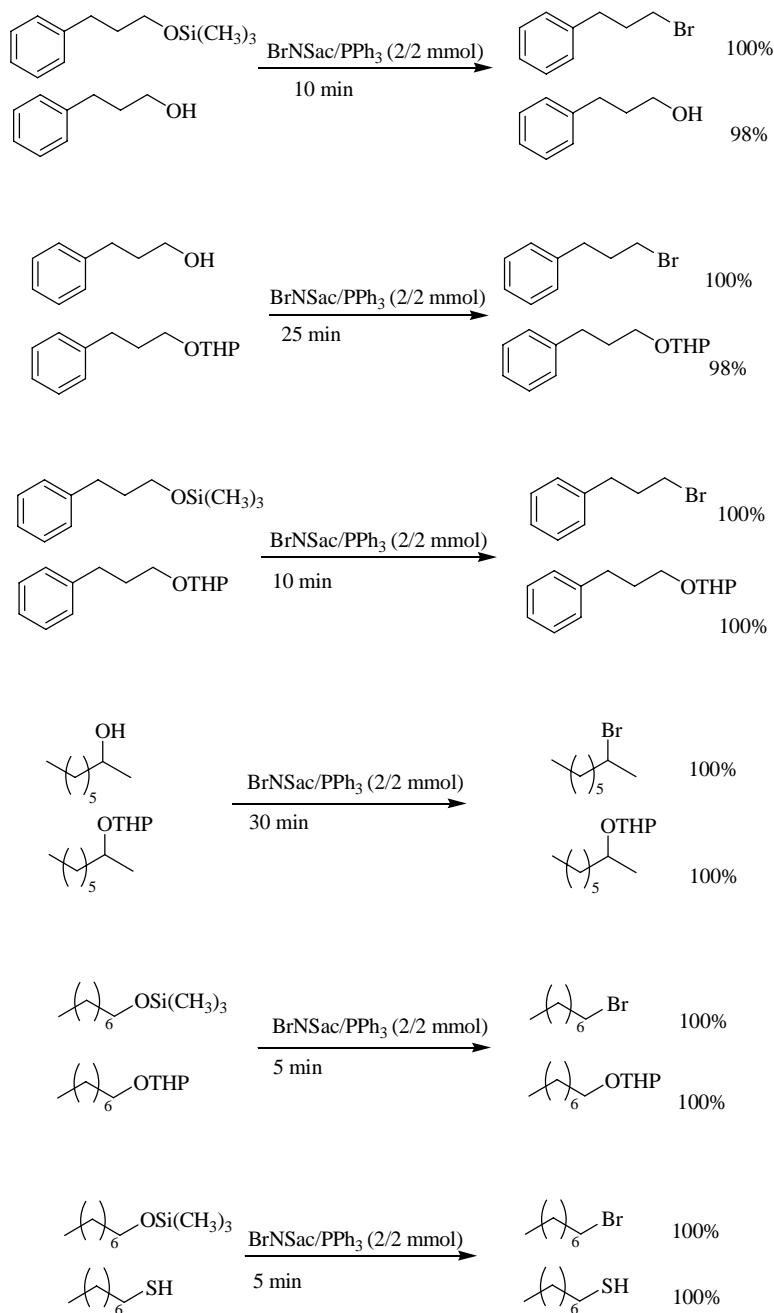
conversion of alcohols, silyl ethers and tetrahydropyranyl ethers into their halides in the presence of each other. The model reactions are shown in Scheme 2.

In conclusion, in this study we have introduced a new, mild, efficient and simple method for the bromination and iodination of structurally diverse trimethylsilyl and tetrahydropyranyl ethers under neutral conditions. The selectivity of the method is excellent and worthy of mention.

Saccharin, which is an edible, non-toxic, commercially available and a cheap material is produced in the reaction mixture can be isolated and halogenated easily for reusing in the similar reactions.

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Scheme 2. Selective reaction of different binary mixtures with $\text{Ph}_3\text{P}/\text{XNSac}$ change NBSac to BrNSac.

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