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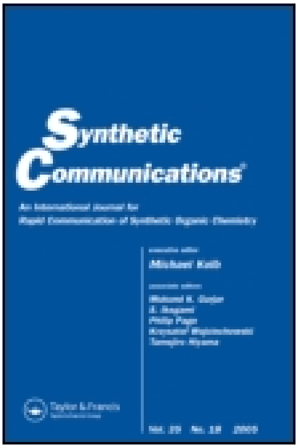

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Published online: 16 Aug 2006.

To cite this article: Wang Sufang , Wang Shaobing & Xu Yongshen (2005): Efficient Synthesis of Trimethylsilyl Pseudohalides Catalyzed by PEG400/ZnI$_2$ under Ultrasound Irradiation, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 35:9, 1271-1276

To link to this article: http://dx.doi.org/10.1081/SCC-200054856

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Synthetic Communications®, 35: 1271–1276, 2005
Copyright © Taylor & Francis, Inc.
ISSN 0039-7911 print/1532-2432 online
DOI: 10.1081/SCC-200054856

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Efficient Synthesis of Trimethylsilyl Pseudohalides Catalyzed by PEG400/ZnI_2 under Ultrasound Irradiation

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Abstract: Trimethylsilyl pseudohalides Me_3SiX, where X = NCS, NCO, or CN, were readily prepared conveniently in desirable yields by the reaction of Me_3SiCl with NaX or KX catalyzed by PEG400 and zinc iodide under ultrasound irradiation.

Keywords: Trimethylsilyl pseudohalides, trimethylsilyl chloride, PEG400, ultrasound irradiation

Trimethylsilyl pseudohalides play important roles in a variety of synthetic transformations. For example, trimethylsilyl cyanide is an effective reagent for the preparation of β-amino alcohols, α-aminonitriles, and α-trimethylsiloxyacrylonitriles from the corresponding ketones, imines, and ketenes.[1] It can also react rapidly with the carbonyl of aldehydes to give silylated

Received in Japan November 10, 2004

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cyanohydrins, which have found to be useful as acyl anion equivalents in many synthetic reactions.[2] Trimethylsilyl isothiocyanate has been widely accepted as an efficient reagent for the C-terminal sequencing of proteins and peptides.[3] Trimethylsilyl isocyanate has been applied to the synthesis of primary amides from Grignard reagent.[4] In summary, trimethylsilyl pseudohalides are a class of important and useful reagents and a great deal of attention has been devoted to their versatile applications.

This class of compounds cannot be readily prepared by mixing up the trimethylsilyl chloride and the pseudohalides salts. The well-established method for the synthesis of this class of compounds was based on the reaction between the alkylsilyl chlorides and their corresponding silver salts.[5] However, the silver salts are expensive and not commonly available, and a high reaction temperature was always required. Although the method for preparing trimethylsilyl cyanides using potassium salts impregnated on the amberlite XAD resin gave excellent yields,[6] the preprocessing of the impregnation of the salts on the expensive resin is troublesome. An alternative method reported for the preparation of trimethylsilyl cyanide and isothiocyanate involved the interaction between bis[trimethylsilyl] sulfate and urea with the expensive N-methylpyrrolidinone as solvent.[7] As far as those drawbacks concerned, some other cheaper and more available pseudohalides sources, such as their potassium or sodium salts, and mild reaction conditions should be more preferable.

Polyethylene glycols (PEGs) can be regarded as the open-chained crown ether and have been used as solvation promoter or phase transfer catalyst (PTC) in many organic reactions owing to their stability, low cost, environmental friendliness, and easy availability.[8,9] In many cases, they are good substitutes for the traditional PTCs, such as the crown ether, which is toxic and expensive, and quaternary ammonium salts or quaternary phosphonium compounds, which are predominantly used in the liquid–liquid two-phase reaction. In contrast with crown ethers, they have a more powerful ability to solubilize the inorganic salts in nonpolar organic solvent because they have two terminal polar hydroxyl groups. For example, it has been reported that 100 ml of PEG400 could dissolve 10 g of potassium thioacetate at room temperature.[10]For the sake of these merits of PEG, we came to study the synthesis of trialkylsilyl pseudohalides by the phase-transfer catalyst PEG400. Because water is not permitted to be involved in the reaction system (because both trialkylsilyl chlorides and the trialkylsilyl pseudohalides are sensitive to water), we envisage that the catalytic amount of PEG400 should first play the role of water to promote the solvolytic dissociation of the inorganic salts by attacking its crystal lattice and should second act as PTC to enhance the reaction rate.

We selected trimethylsilyl chloride and potassium cyanide as the starting material to synthesize trimethylsilyl cyanide in dichloromethane in presence of PEG400 under stirring at room temperature to study the general method for the preparation of this class of compounds. However, only 40% of trimethylsilyl

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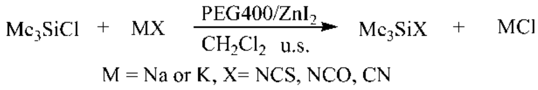
cyanide was obtained after the mixture was stirred for 24 h when 5% mol of PEG400 was dosed and 10% of potassium cyanide was overdosed based on trimethylsilyl chloride. Then, we thought about adding some Lewis acid to enhance the reaction rate. Several Lewis acids were used and the comparative experiments showed that zinc iodide exhibited the best catalytic effeciency, from which we deduced that the participation of the iodine anion might play a role by enhancing the rate of SN2 (Substitution Nucleophilic Bimolecular) substitution. Seventy-five percent of trimethylsilyl cyanide was achieved after the reaction was performed for 20 h with the introduction of 0.5% of ZnI_2, which indicated that the introduction of the catalytic amount of ZnI_2 could greatly enhance the reaction rate and the product yield (Scheme 1). However, the reaction time was still much longer than expected. It should be pointed out that as the reaction proceeded, the trialkylsilyl chlorides would react with the one or two terminal hydroxyl groups of PEG400 to give the PEG400-silyated ether. The longer the reaction time, the more PEG400 was silyated. Although the formed PEG400-silyated ether still possessed the phase-transfer ability because it is also an analogue of acyclic ether, its ability of dissociating the inorganic salts to give the negative nucleophile must decrease with the loss of the hydroxyl groups.

It was reported in the previous literature that the ultrasonic irradiation could play the role of promoting the solvolytic dissociation of the inorganic salts by attacking its crystal lattice.[11] Based on this theory, we also introduce the ultrasound irradiation into the experiment to promote the dissociation of the salts of pseudohalides. As a result, the reaction time was greatly enhanced compared with the experiment under stirring. The other two trimethylsilyl pseuodohalides, trimethylsilyl isothiocynate and trimethylsilyl isocyante, were also prepared in the similar manner. The results are summarized in Table 1.

The readily available and recoverable dichloromethane was used as solvent and the reaction was performed under ultrasound irradiaton in the presence of catalytic amounts of PEG400 and zinc iodide. An excess (20%) of dried and powdered inorganic pseudohalide salts was used for ensuring the complete conversion of the reactants. The comparative experiments showed that the lower dosage of PEG400 could not catalyze the reaction effectively, so an appropriate amount of PEG400 (5% mol) is necessary to ensure better catalytic ability.

It can be shown from Table 1 that the presence of a catalytic amount of Lewis acid obviously enhanced the reaction rate and improved the overall yield. This might be explained by the fact that Lewis acid could enhance



$$Mc_3SiCl + MX \xrightarrow[CH_2Cl_2\ u.s.]{PEG400/ZnI_2} Mc_3SiX + MCl$$

M = Na or K, X= NCS, NCO, CN

Scheme 1.

Table 1. Nucleophilic substitution of trimethylsilyl pseudohalides in CH_2Cl_2 catalyzed by PEG400 and Lewis acid under ultrasound irradiation[a]

Entry	Salt	Product	Catalyst	Time (h)	Yield (%)[b]
1	NaCN	$(CH_3)_3SiCN$	none	20	15
2	NaCN	$(CH_3)_3SiCN$	$AlCl_3$	7	48
3	NaCN	$(CH_3)_3SiCN$	$ZnCl_2$	7	45
4	NaCN	$(CH_3)_3SiCN$	$ZnBr_2$	6	46
5	NaCN	$(CH_3)_3SiCN$	ZnI_2	4	80
6[c]	NaCN	$(CH_3)_3SiCN$	ZnI_2	16	78
7	NaOCN	$(CH_3)_3SiNCO$	ZnI_2	3.5	85
8	KSCN	$(CH_3)_3SiNCS$	ZnI_2	5	86

[a] All the experiments were performed in a hood with good ventilation.

[b] Yield of isolated products is calculated according to trialkylsilyl chlorides.

[c] The reaction was performed under stirring for comparison purpose.

the break up of the Si–Cl bond and thus make it easier for the nucleophine to attack the positive polarized Si. However, the catalytic effects of the different Lewis acid vary under the same condition. Among the three Lewis acids, zinc iodide showed the best catalytic ability, which might be explained by the fact that iodide anion always showed excellent catalytic effect in an SN2 reaction.

CH_2Cl_2 is an ideal solvent for the reaction in that it is miscible with PEG400, recyclable, and has a boiling point much lower than that of the product, which can ensure an effective separation. It is worthy of note that trimethylsilyl azide, although belonging to this class of compoud, should not be prepared by this method because the inorganic azide salts are prone to explode under ultrasound irradiation.

In a comparative experiment concerning the reaction between trimethylsilyl chloride with sodium cyanide, it was found that the reaction under catalysis of metal iodide and ultrasound irradiation without PEG400 did not take place. From this, a conclusion can be drawn that both PEG400 and metal iodide play important roles in the conversion of the reaction; the importance of the former is primary and the utilization of the ultrasound irradiation could greatly shorten the reaction time.

In conclusion, we have found a convenient method for the preparation of trimethylsilyl pseudohalides catalyzed by PEG400/ZnI_2 under ultrasound irradiation with the advantages of cheaper and more readily available reagents, recoverability of the solvent, and the simplicity of the workup.

EXPERIMENTAL

GC: GC-17A with 2 m of column silicon-SE-30. A national ultrasound cleanser operating at 40 MHz was used. TMSCl was freshly distilled.

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Potassium cyanide was finely grounded and dried at 120°C under vacuum for 6 h. PEG400 and zinc iodide are commercially available and used directly without further disposal.

Procedure for the Preparation of TMSNCS

A 100 ml, three-necked, round-bottomed flask equipped with nitrogen inlet tube was charged successively with 0.5 g of ZnI_2, 30 ml of CH_2Cl_2, 2 g (0.005 mol) of PEG400, 7.8 g (0.12 mol) of potassium thiocyanide, and 12 g (0.11 mol) of TMSCl. The mixture was partly immersed into the ultrasound cleanser thermostated at 20°C for the period of time designated in Table.1 The process of the reaction was monitored by GC. After the completion of the reaction, the inorganic solids were filtered off and washed with small amount of dried CH_2Cl_2. After dichloromethane was distilled through a 5-cm Vigreux column, 8.5 g of TMSCN was collected at 142–144°C (lit.[5] bp 143–144°C). Yield, 86%; purity by GC, 99.5%; IR (KBr, γcm^{-1}): 435, 634, 764, 845, 956, 1257, 1952, 2072, 2964. EI-MS (m/z): 132, 131, 116, 88, 86, 73, 43.

TMSNCO was prepared in the same fashion as described for TMSNCS. Bp 90–93°C (lit.[5] bp 90–92°C); yield, 86%; purity by GC, 98.5%; IR (KBr, γcm^{-1}): 525, 620, 645, 761, 850, 1258, 1432, 2281, 2965, 3698. EI-MS (m/z): 115, 100, 72, 70, 43.

TMSCN was prepared in the same fashion as described for TMSNCS. Bp 115–117°C. (lit.[5] bp 114–117°C); yield, 78%; purity by GC, 99.5%; IR (KBr, γcm^{-1}): 640, 770, 855, 1260, 1420, 2190, 2905, 2970. EI-MS (m/z): 99, 84, 73, 54, 43.

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