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A study on the heterogeneous reaction of trialkylsilyl chlorides with inorganic salts and monocarboxylates catalysed by PEG400

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The important and useful trialkylsilyl pseudohalides R_3SiX, where X=NCS, NCO, N_3 or CN and R=methyl or ethyl, and trimethylsilyl monocarboxylates, where X=RCOO, were readily prepared in high yields by nucleophilic substitution of R_3SiCl with X ions provided by NaX or KX at room temperature catalysed by PEG400 and zinc iodide. The reactions of trimethylsilyl chloride with some metal oxysalts were also studied for the first time.

Keywords: trialkylsilyl chloride; trialkylsilyl pseudohalides; PEG400; trimethylsilyl monocarboxylates; hexamethyldisiloxane

Trialkylsilyl pseudohalides have played important roles in a variety of synthetic transformations and a great deal of attention has been devoted to their versatile applications. They are always deemed as mild and stable nucleophiles, acting formally as the corresponding organometallics.[1] For example, in addition to having been widely accepted as an efficient reagent for the C-terminal sequencing of proteins and peptides,[2] trimethylsilyl isothiocyanate has been successfully used for the synthesis of oxazolidin-2-thione, which shows interesting biological activity and can also be acted as chiral auxiliaries.[3] Trimethylsilyl azide, in many cases used as a substitute of the explosive hydrazoic acid, can undergo substitution reactions with acid chlorides to form acyl azides, which are useful precursors for the synthesis of isocyanates.[4] Trimethylsilyl isocyanate has been applied to the synthesis of primary amides from Grignard reagents.[5] In addition, the selective reaction of trimethylsilyl cyanide with α,β-unsaturated ketones to afford the corresponding 1,2- adducts without the formation of 1,4-adducts has also been reported.[6]

The traditional method reported for the synthesis of the trialkylsilyl pseudohalides was based on the interaction between alkylsilyl chlorides and the corresponding silver salts of the pseudo halide.[7] However, it is not economical to put the method into large-scale production since silver salts are expensive and not commonly available, and a high-reaction temperature is always required. Although the method for preparing trialkylsilyl azides and cyanides using potassium or sodium salts impregnated on Amberlite XAD resin gave excellent yields,[8,9] the pre-impregnation of the salts on the expensive resin is troublesome. The other 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.[10]

$$R_3Si{-}Cl \;+\; MX \xrightarrow[CH_2Cl_2\ \ r.t]{PEG400/ZnI_2} R_3Si{-}X \;+\; MCl$$

R = methyl or ethyl, M = Na or K X = NCS, NCO, CN or N_3

Scheme 1

As far as those drawbacks concerned, some other cheaper and more available pseudohalides sources, such as their potassium or sodium salts, and mild reaction condition should be preferable for the preparation of this useful class of compounds.

Until now, the application of PTCs has drawn a great deal of attention, and substantial interest has been devoted to the utilisation of polyethylene glycols (PEGs), considered in some instances as acyclic crown ether analogous, as PTCs or solvation promoters for various reactions.[11] Attractive features of PEGs include their low cost, readily availability and apparent lack of significant toxicological properties. In many cases, they are good alternative 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 a liquid–liquid two-phase reaction. In contrast with crown ethers, they have more powerful ability to solubilise the inorganic salts in a non-polar organic solvent due to the fact that they have two terminal polar hydroxyl groups. In continuation of our research on the use of PEGs as PTC,[12] we now report a facile method for the preparation of trialkylsilyl pseudohalides by the nucleophilic substitution of trialkylsilyl chlorides with potassium or sodium pseudohalides salts. The results are summarised in Table 1.

The readily available and recoverable dichloromethane was used as solvent and the reaction was performed by stirring at room temperature in the presence of catalytic amount of

Table 1 Nucleophilic substitution of different trialkylsilyl pseudohalides in CH_2Cl_2[a]

Entry	R	Salt	Product	Time/h	Yield/%[b]	B. p. (°C/mmHg)	
						Found	Reported
1	Methyl	NaOCN	$(CH_3)_3SiNCO$	3.5	93	90–93	90–92[7]
2	Methyl	KSCN	$(CH_3)_3SiNCS$	5	92	142–144	143–144[7]
3	Methyl	NaN_3	$(CH_3)_3SiN_3$	6	90	95–97	92–97[8]
4	Methyl	NaCN	$(CH_3)_3SiCN$	16	83	115–117	114–117[7]
5	Ethyl	NaOCN	$(C_2H_5)_3SiNCO$	4	90	88–90/70	163–167[7]
6	Ethyl	KSCN	$(C_2H_5)_3SiNCS$	6.5	88	116–118/50	209–211[7]
7	Ethyl	NaN_3	$(C_2H_5)_3SiN_3$	7	85	90–92/60	97–99/80[8]
8	Ethyl	NaCN	$(C_2H_5)_3SiCN$	20	80	96–98/50	180–185[7]
9	Methyl	CH_3CO_2Na	$CH_3CO_2Si(CH_3)_3$	1.5	96	102–104	102–104[16]
10	Methyl	$CH_3CH_2CO_2Na$	$CH_3CH_2CO_2Si(CH_3)_3$	1	94	120–123	120–122[17]
11	Methyl	$C_6H_5CO_2Na$	$C_6H_5CO_2Si(CH_3)_3$	2	93	221–223	221[18]

[a] All the experiments were performed in a hood with good ventilation.
[b] Yield of isolated products calculated according to trialkylsilyl chlorides.

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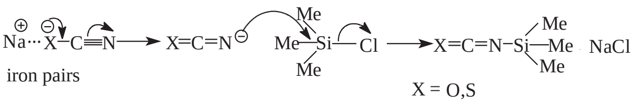
PEG400 and zinc iodide. An excess (20%) of dried and powdered inorganic pseudohalides salts was necessary for ensuring the complete conversion of the reactants. In order to find out whether the reaction followed an S_N1 or S_N2 mechnism, both trimethylsilyl chloride (TMSCl) and triethylsilyl chloride were used as substrates. It can be seen from the results that for the same nucleophile, the reactions involving triethylsilyl chloride always needed longer reaction times, which we proposed resulted from the steric hindrance of the bulky ethyl groups. Based on this, we proposed that the designation of the mechanism for this type of reaction should follow the S_N2 route. As it can be seen from Table 1, the reaction times in entries 4 and 8 were relatively longer than that in the other cases, which indicated that CN^- was a weaker nucleophile and thus needed longer reaction times. Generally, according to the increasing reaction time, we proposed that the nucleophilicity of different nucleophiles follow the order $OCN^- > SCN^- > N_3^- > CN^-$. Since the aprotic solvent CH_2Cl_2 was used, we assumed that the dissolved ionic compounds were likely to present as ion pairs. It is worth noting that the formation of trialkylsilyl isocyanate and isothiocyanate was related to the ambident character of the ^-SCN and ^-OCN anions, and we proposed that the negative charge on the oxygen atom will be more easily transferred to the nitrogen atom than that on the sulfur atom, in that the atomic size of oxygen, compared with that of sulfur, is much closer to the atomic, size of carbon, which made the conjugation more effective (Scheme 2).

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. So the overdosing of PEG400 would inevitably consume more alkylsily chlorides and reduce the overall yields. However, since the reaction was performed at room temperature and only a catalytic amount of PEG400 was dosed, the byproduct thus formed was negligible. On the other hand, we propose that the formed PEG400-silyated ether still possess phase transfer ability since it is also an analogue of an acyclic ether. Generally it was found that smaller dosage of PEG400 could not catalyse the reaction effectively. In conclusion, an appropriate dosage of PEG400 (2–3%) was suitable. With the introduction of zinc iodide, we found that in all cases, especially in the case of preparing trialkylsilyl cyanides, the reaction rate was remarkably enhanced compared with the case without the participation of zinc iodide. Among the several solvents we used for selection, dichloromethane was found to be a desirable solvent for the reaction in that it was miscible with PEG400, and has a low boiling point, which could ensure the excellent separation of the products.

The method described above is also suitable for the preparation of trimethylsilyl carboxylates. Sodium acetate, propionate, and benzoate were found to react smoothly with TMSCl catalysed by PEG400 and zinc iodide at room temperature to afford trimethylsilyl monocarboxylates, which are very useful reagents in organic synthesis.[13,14] The experimental results were integrated into Table 1.

In an attempt to replace the chlorine atom by the nitroso- and nitro- groups, we also examined the interaction of TMSCl with sodium nitrite or sodium nitrate in the presence of PEG400 and zinc iodide. However, no aimed trimethylsilyl nitrite or trimethylsilyl nitrate was obtained in each case. We found surprisingly that hexamethyldisiloxane, confirmed by comparing its boiling point and IR data with that in the literature[15], was formed, with the release of gases with an irritating odour in both cases during the reaction. We propose that the formed gases should be nitrogen oxides, but there is no further confirmation on this point. Comparative experiments with and without the participation of zinc iodide were carried out in order to study whether zinc iodide will undergo redox reaction with the sodium nitrite and nitrate. The results showed that no obvious side reaction was found and the reaction time was slightly shortened with the participation of zinc iodide.



Scheme 2

Out of curiosity, we studied the interaction between TMSCl with some inorganic salts. Both Na_2CO_3 and Na_2SO_3 were found react smoothly with TMSCl catalysed by PEG400 at room temperature with the release of gases, even without the participation of zinc idode. Hexamethyldisiloxane was confirmed by melting point and IR data to be the common products. The collected gases in both cases could turn lime water turn milky and the gas emitted in the later case has an irritating odour of sulfur dioxide. Based on this, we propose that the gases should be carbon dioxide and sulfur dioxide respectively, but there is no further confirmation on this point. However, it was found that sulfate did not react with TMSCl, which was nearly quantitatively recovered after the reaction was performed for 24 h under reflux in the presence of PEG400 and zinc iodide.

When the reaction of 0.8g of TMSCl with 1g of $KClO_3$ in 20 ml of CH_2Cl_2 was performed in the presence of PEG400 and zinc iodide, the reaction mixture was found to become yellow gradually, and gas with chlorine odour was continuously emitted from the reaction vessel. When the gas was collected over distilled iced water, a yellow–green solution was formed.

> **CAUTION:** An explosion broke out and the reaction flask was totally destroyed when we enlarged the dosage of the starting materials to four times that of the first case, whilst keeping the amount of 20 ml of CH_2Cl_2 unchanged. Later when 40 ml of CH_2Cl_2 was used and nitrogen gas was bubbled into the flask to dilute and drive away the formed gas, no explosion occurred.

When the aqueous solution of the gas was used for spectroanalysis, it showed strong absorbances at 360nm in its UV spectrum and $1090cm^{-1}$ in its IR spectrum. By comparison, we found that aqueous solutions of chlorine showed no absorbance at these two wavelengths. These two spectrographic data, according to the previous literature reports,[19] were basically in agreement with that of ClO_2. Based on these findings, we proposed that the formed gas might be the explosive ClO_2, and the explosion was caused by its accumulation and decomposition. We also found that the other nongaseous product, apart from potassium chloride, was collected by distillation at 112–114°C. Based on the basic agreement of its boiling point and IR analysis with those in the literature,[20] we propose it should be hexamethyldisilane, not hexamethldisiloxane, which we initially assumed should be the final product. However, much more work is needed to define the reaction mechanism.

In summary, we have found a convenient method for the preparation of trialkylsilyl pseudohalides and trimethylsilyl monocarboxylates catalysed by PEG400, with advantages of lower reaction temperature, cheaper and more readily available reagents, recoverability of the solvent and the simplicity of the work up. A preliminary study on the reaction between TMSCl and $NaNO_3$, $NaNO_2$, $NaSO_3$ or $KClO_3$ has also been reported for the first time.

Experimental

GC: GC-17A with 2m of column silicon-SE-30. The solvents were refined according to the literature. TMSCl was freshly distilled. Potassium cyanide was finely grounded and dried at 120°C under vacuum for 6 hours. PEG400 and zinc iodide are commercially available.

The general procedure for the preparation of TMSNCS: A mixture of 0.25g of zinc iodide, 40ml of CH_2Cl_2, 17.5 g (0.18 mol) of potassium isothiocyanate, 2g (0.005 mol) of PEG400 and 16g (0.15 mol) of TMSCl was vigorously stirred under nitrogen atmosphere at room temperature for 5 h. The process of the reaction was monitored by GC. After the completion of the reaction, the solid was filtered and meticulously washed with dried CH_2Cl_2. After CH_2Cl_2 was recovered from the combined filtrate, the residual solution was distilled through a 5cm Vigreux column. 18.1g (92%) of TMSNCS was collected at 142–144°C.

The general procedure for the preparation of trimethylsilyl acetate: 8g (0.075 mol) of TMSCl was added dropwise to the mixture of 0.10g of zinc ioddide, 20ml of CH_2Cl_2, 1g (0.0025 mol) of PEG400 and 6.15g (0.075 mol) sodium acetate within 30 minutes, and the mixture was kept stirred at room temperature for 1 h. The process of the reaction was monitored by GC. When the reaction was finished, the solid was filtered and washed with dried CH_2Cl_2. After the recycle of CH_2Cl_2, the residual solution was distilled through a 5cm Vigreux column. 9.5g (96%) of trimethylsilyl acetate was collected at 102–104°C.

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