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Thiocyanation of alkyl halides with alkyl thiocyanates in the presence of quaternary phosphonium halides

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Alkyl thiocyanates undergo simple S_N2 reactions with the counter ions of quaternary phosphonium salts in nonpolar solvents and thiocyanate ions are liberated as the leaving ion. Depending on the nucleophile, the reaction proceeded irreversibly or reversibly. The reaction of benzyl thiocyanate with azide ions afforded a quantitative yield of benzyl azide. The reactions of alkyl thiocyanates with halide ions gave an equilibrium mixture where the reverse reaction of the alkyl halides produced with the liberated thiocyanate ions took place simultaneously. Thus, thiocyanate–halide exchange reactions between an alkyl thiocyanate and an alkyl halide were possible in the presence of a catalytic amount of a quaternary salt.

Introduction

Alkyl thiocyanates have been conveniently prepared from the corresponding alkyl halides, sulfates, or sulfonates by reaction with an alkali-metal thiocyanate.[1] Phase-transfer catalysis or supported reagent methodology has also been applied to these syntheses.[2–6] Alkyl thiocyanates can undergo several reaction types since the thiocyanate group has a diversity of reactive sites within the SCN group. Soft nucleophiles may attack the sulfur atom to induce S–CN bond fission.[7,8] Reaction with hydroxide ion, alkoxide ion, or amines may occur at the cyano carbon atom with the displacement of a thiolate ion. To date however, substitution of the thiocyanate group by nucleophiles has not been commonly reported except for with some activated organic thiocyanates such as 2,4-dinitro-1-thiocyanatobenzene[9] or 1-methyl-4-thiocyanatouracil.[10] In the course of our studies on polymer-supported phase-transfer catalysis,[11–13] we have noticed that a particular alkyl thiocyanate appears to react with polymer-supported iodide ions to give the corresponding alkyl iodide though its yield is very low. This prompted us to examine the reaction of thiocyanates with the counter-anions of quaternary phosphonium salts. In this article, we demonstrate that, in nonpolar solvents, alkyl thiocyanates undergo simple bimolecular nucleophilic substitutions with halide ions as well as other common nucleophiles and that the exchange of halide and thiocyanate groups between alkyl halides and alkyl thiocyanates takes place smoothly in the presence of halide ions.

Experimental

Materials and equipment

^{1}H NMR spectra were recorded on a Varian Gemini 300H, 300 MHz spectrometer. GLC analyses were carried out on a Hitachi Model 263 FID instrument with a 1 m column of SE-30 or PEG-20M.

(1) Quaternary salts. Hexadecyltributylphosphonium bromide (HTBPB) was purchased from Tokyo-Kasei and was used without further purification. Hexadecyltributylphosphonium chloride (HTBPC) and benzyltributylphosphonium chloride (BTBPC) were prepared by the quaternization of tributylphosphine with hexadecyl chloride and benzyl chloride, respectively in toluene at 90 °C for 72 h. Hexadecyltributylphosphonium azide (HTBPA) was prepared by the ion-exchange method using an anion-exchange resin, Amberlite IRA400. The anion exchange resin was transformed into the azide form by treatment with an excess of 1.0 mol L^{-1} sodium azide aqueous solution. The resin was packed in a 20 cm column. Then a 7.5 mL of a solution of HTBPB in methanol (0.5 mol L^{-1}) was passed through the column using methanol as eluent. The methanol solution was passed three times through the azide-formed resin. After the methanol solution was dried on molecular sieves, it was evaporated and the remaining white solid was dried *in vacuo*. Hexadecyltributylphosphonium dimethyldithiocarbamate was prepared through the ion exchange of HTBPB with an excess of sodium dimethyldithiocarbamate in methanol. The methanol solution was treated with toluene and then hexane. The sodium dimethyldithiocarbamate precipitated was filtrated off and the filtrate was evaporated. The white solid obtained was dried *in vacuo*. The purities of the prepared phosphonium salts were determined by the GLC analyses of decyl derivatives that were formed by the reaction of decyl methanesulfonate with the phosphonium salts. All the phosphonium salts had purities greater than 98%. The water content of the phosphonium salts was determined by ^{1}H NMR analysis. The quantity of water is represented as w, which is the molar ratio of water to phosphonium salt.

The polystyrene-attached phosphonium salts were prepared by the reaction of tributylphosphine with a cross-linked polystyrene containing chloromethyl groups (1% divinylbenzene, active chloride 1.00 mmol g^{-1}).[12]

(2) Alkyl thiocyanate. Benzyl thiocyanate and methyl thiocyanate were purchased from Tokyo-Kasei and Kanto-Kagaku, respectively, and were used without further purification. Butyl thiocyanate was prepared by the phase-transfer catalytic reaction between butyl bromide and aqueous potassium thiocyanate using trioctylmethylammonium chloride (TOMAC) and was purified by distillation under reduced pressure. δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.97 (3H, t, C(3)Me), 1.50 (2H, m, C(3)H), 1.81 (2H, m, C(2)H), 2.95 (2H, t, C(1)H) and δ_H(300 MHz; C_6D_6; Me_4Si) 0.62 (3H, t, C(3)Me), 0.91 (2H, m, C(3)H), 1.26 (2H, m, C(2)H), 2.09 (2H, t, C(1)H). Decyl thiocyanate

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was prepared in the same way. δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.88 (3H, t, C(9)Me), 1.28–1.52 (14H, m, C(9)H–C(3)H), 1.82 (2H, m, C(2)H), 2.94 (2H, t, C(1)H) and δ_H(300 MHz; C_6D_6; Me_4Si) 0.94 (3H, t, C(9)Me), 1.1–1.6 (16H, m, C(9)H–C(2)H), 2.09 (2H, t, C(1)H).

(3) Authentic samples. Benzyl chloride, benzyl bromide, and benzyl acetate from Nacalai-Tesque, butyl iodide from Wako Chemicals, and decyl chloride and decyl bromide from Tokyo-Kasei were used without further purification. Benzyl azide was prepared by the reaction of benzyl chloride with sodium azide in ethanol at 60 °C. δ_H(300 MHz; $CDCl_3$; Me_4Si) 4.33 (2H, s, CH_2), 7.3–7.6 (5H, m, Ph). Benzyl dimethyldithiocarbamate was prepared by the reaction of benzyl chloride with sodium dimethyldithiocarbamate dihydrate in ethanol at 60 °C in the dark. δ_H(300 MHz; $CDCl_3$; Me_4Si) 3.46 (6H, d, NMe_2), 4.55 (2H, s, CH_2), 7.2–7.4 (5H, m, Ph). Benzyl iodide and decyl iodide were prepared by the reaction of the corresponding alkyl bromide with aqueous potassium iodide using the usual phase-transfer catalysis method.

Kinetics

(1) NMR method. A 5 mm internal diameter NMR tube with a polypropyrene cap was charged with 50 µL of a solution containing a given amount of quaternary salt, 0.7 mL of a deuteriated solvent, and a prescribed amount of water. The tube was stirred to make a homogeneous solution at 60 °C, followed by injection of 50 µL of a solution containing a given amount of the alkyl thiocyanate *via* a micropipette. The reaction was monitored throughout in the NMR probe at 60 °C. The α-methylene peaks of the substrate and product were integrated periodically to obtain the conversion. Each peak in the reaction mixture moved slightly within ±0.05 ppm from the position that it was observed in the absence of quaternary salts. The product was thus identified by finally adding an authentic sample to the reaction mixture. The chemical shifts actually observed for each reaction are given in the corresponding table or figure using the residual protons contained in the deuteriated solvent as a reference; δ_H 7.20 (C_6D_6), 7.25 ($CDCl_3$), 3.35 (CD_3OD), and 2.50 (DMSO). Second-order kinetics were followed up to 90% completion when the reactions were irreversible. The reactions followed eqn. (1) and the second-order rate constants (k_2) were

$$1/(a-b)\ln\left[b(a-x)/a(b-x)\right] = k_2 t \qquad (1)$$

calculated using a least-squares method, where a, b, and x represent the initial concentrations of thiocyanate and phosphonium salts, and the concentration of the product at time t, respectively. All rate determinations involved at least 6 points plotted and gave correlation coefficients of 0.998 or better. The rate of reaction between hexadecyltributylphosphonium azide and benzyl thiocyanate was reproducible within ±5% error.

When the reactions were reversible, the equilibrium constants (K) were calculated using eqn. (2). The second-order rate

$$K = x_e^2/(a-x_e)(b-x_e) = k_2/k_{2-} \qquad (2)$$

constants (k_2 and k_{2-}) for the forward and reverse reactions were calculated using a least-squares method based on eqn. (3),

$$1/[2x_e(1-K^{-1})-(a+b)]\ln(1-y)/[1-y(\alpha-1)] = k_2 t \qquad (3)$$

where x_e is the concentration of products at equilibrium, $y = x/x_e$, and $\alpha = (1/a + 1/b)x_e$. The equilibrium constant of the reaction between benzyl thiocyanate and HTBPC was reproduced within ±50% on runs of different initial concentrations of the substrate and reagent while a clear linear line of eqn. (3) was obtained for each run with a correlation coefficient of 0.993 or better. Thus the values of k_2 and k_{2-} in the tables are estimated to contain less than 50% error.

(2) GC method. The general procedure is as follows. A 30 mL culture tube with a Teflon-lined screw cap was charged with prescribed amounts of resin with 0.05 mmol of the phosphonium salt, inorganic reagent plus prescribed amounts of water, and 2 mL of an organic solvent containing pentadecane as an internal standard. The tube was placed in an oil bath maintained at 90 °C and the mixture was stirred for 30 min with a Teflon-coated magnetic stirring bar, followed by injection of 70 µL of the alkyl thiocyanate *via* a micropipette. Aliquots of the organic layer were withdrawn periodically with a microsyringe to determine the concentrations of the substrate and product by GLC.

Results and discussion

Reversible and irreversible nucleophilic reactions

We first examined homogeneous reactions of benzyl thiocyanate with soluble phosphonium salts in benzene-d_6 under anhydrous conditions. The reactions were carried out at 60 °C in the presence of an excess of phosphonium salt. With hexadecyltributylphosphonium azide (HTBPA), ^1H NMR analysis showed that a decrease in the benzyl thiocyanate concentration was accompanied by the formation of the corresponding benzyl azide as shown in Fig. 1. No other product was detected. This means that the azide ions of the phosphonium salt act as a nucleophile and selectively attack the α-alkyl carbon of the thiocyanate, leading to a release of thiocyanate ions. The conversion is plotted against time in Fig. 2. The reaction proceeded irreversibly and a quantitative amount of benzyl azide was finally formed. This result is in striking contrast to the recent report[14] that the reaction of alkyl thiocyanate with azide ions in the presence of ammonium chloride and hexadecyltrimethylammonium bromide affords 5-alkylthiotetrazole. As shown later, this is due to the the presence of other components that play an important role in cycloadditions. The reaction of benzyl thiocyanate with dimethyldithiocarbamate also proceeded irreversibly to give 100% yield of the corresponding substitution product, as also shown in Fig. 2.

On the other hand, as shown in Fig. 3, the reactions of benzyl thiocyanate with hexadecyltributylphosphonium halides (HTBPX: X = Cl, Br, and I) soon attained equilibrium at 60 °C. The initial rate of the reaction was fastest with iodide ions but the yield of benzyl iodide was very low at the chemical equilibrium. It took much more time for chloride to attain the equilibrium though the final conversion was considerably larger than that of bromide or iodide. The products were the corresponding benzyl halides. No other products were detected unless the reaction mixture was allowed to stand for a prolonged time after the equilibrium was attained. This means that the reverse reaction represented by eqn. (4) takes place simultaneously. The reverse reaction is well known as a typical S_N2 reaction.

$$\mathrm{RSCN} + \mathrm{Q^+X^-} \xrightleftharpoons[k_{2-}]{k_2} \mathrm{RX} + \mathrm{Q^+SCN^-} \qquad (4)$$

Rate analyses of second-order kinetics gave the second-order rate constants for both the forward reaction and reverse reaction (see Experimental section). As shown in Table 1, the nucleophilicity towards benzyl thiocyanate, k_2, is the following order in benzene, $Me_2NCSS^- > N_3^- > I^- > Br^- > Cl^-$. A soft ion tends to show a high nucleophilicity to benzyl thiocyanate. Thus, the dimethyldithiocarbamate ion is 10^3 times more reactive than the chloride ion while the reactivity difference among halide ions is relatively small. The second-order rate constants of the corresponding reverse reactions are also shown in Table 1, together with the equilibrium constants of eqn. (4), K ($=k_2/k_{2-}$). As expected, the order of k_{2-} was coincident with the well-known reactivity of the halide leaving groups,

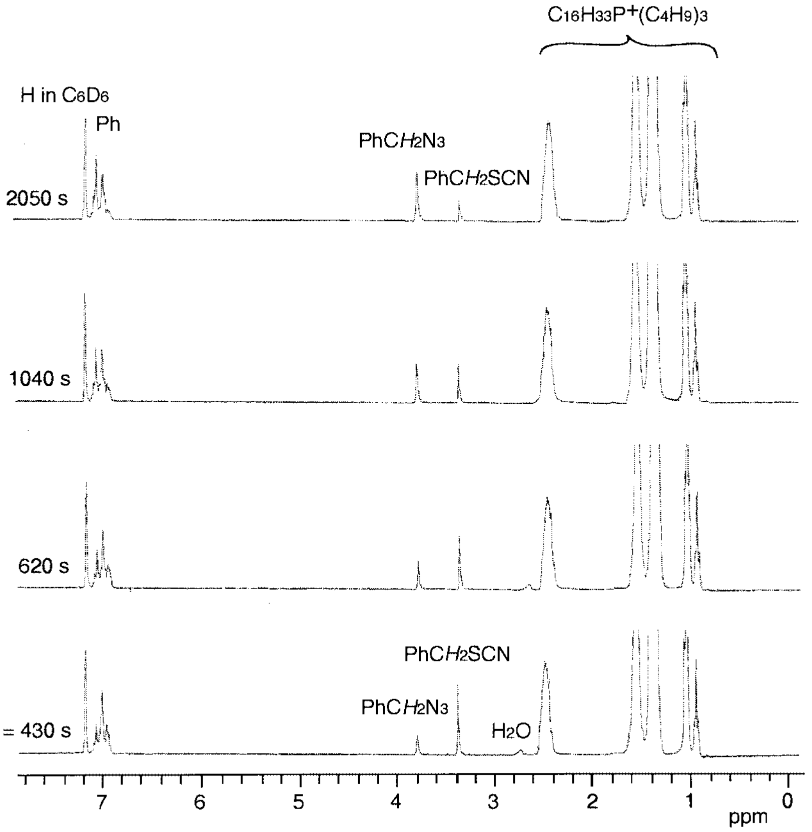

Fig. 1 ^{1}H NMR spectra taken during the reaction of benzyl thiocyanate with hexadecyltributylphosphonium azide in benzene-d$_6$ at 60 °C. *Reaction conditions*: 0.09 mol dm^{-3} of benzyl thiocyanate with 0.11 mol dm^{-3} of hexadecyltributylphosphonium azide and 0.17 of the molar ratio of water to quaternary salt (*w*). The conversions were calculated based on the minor component. The singlet at δ_H 3.39 corresponding to the methylene of benzyl thiocyanate decreased with the reaction time, *t*, and another singlet corresponding to benzyl azide increased at δ_H 3.80.

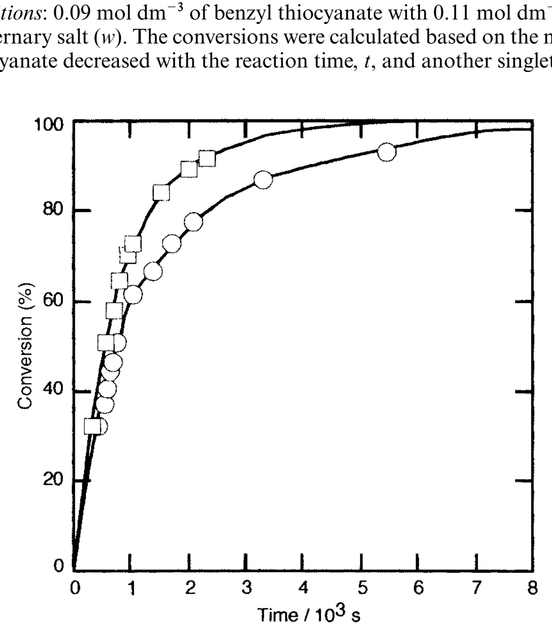

Fig. 2 Conversion plots for the reaction of benzyl thiocyanate with phosphonium salts in benzene-d$_6$ at 60 °C. *Reaction conditions*: 0.09 mol dm^{-3} of benzyl thiocyanate with 0.11 mol dm^{-3} of hexadecyltributylphosphonium azide (○) and 0.0036 mol dm^{-3} of benzyl thiocyanate with 0.0028 mol dm^{-3} of hexadecyltributylphosphonium dimethyldithiocarbamate (□). The conversions were calculated based on the minor component. The singlet peaks of benzyl thiocyanate and benzyl azide appeared at the same chemical shifts as in Fig. 1. When dimethyldithiocarbamate was the reagent, a new singlet peak appeared at δ_H 4.67, which was identified as the methylene proton of benzyl dimethyldithiocarbamate.

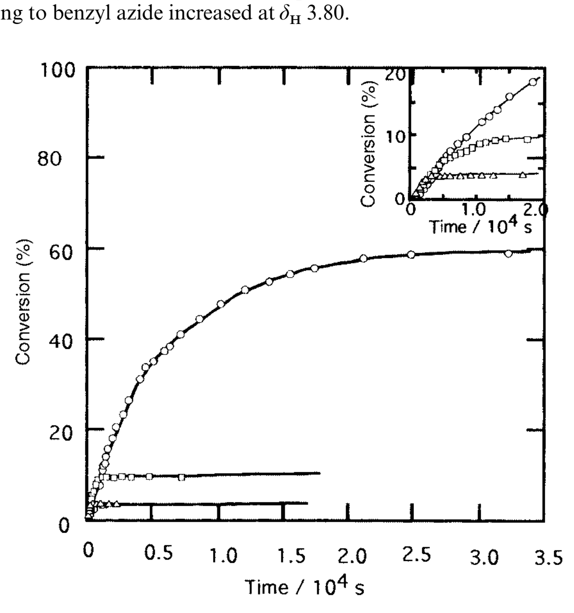

Fig. 3 Conversion plots for the reaction of benzyl thiocyanate with halide ions at 60 °C in benzene-d$_6$. *Reaction conditions*: 0.1 mol dm^{-3} of benzyl thiocyanate with 0.1 mol dm^{-3} of HTBPX; X = Cl (○), Br (□), and I (△). The singlet peaks of the methylene protons were used to follow the reactions; δ_H 3.80 (PhCH_2SCN), 4.18 (PhCH_2Cl), 4.07 (PhCH_2Br), and 4.02 (PhCH_2I).

I > Br > Cl. The equilibrium constant was much lower than unity for HTBPB and HTBPI, in accord with the results that the rate constant of the reverse reaction was much larger than that of the forward reaction. However, chloride ions gave a rate constant for the forward reaction larger than that for the reverse reaction, resulting in an equilibrium constant beyond unity. This means the reaction with chloride would give almost a quantitative amount of benzyl chloride if a large excess of chloride reacted with benzyl thiocyanate.

The reactions of benzyl halides with azide ions were carried out to evaluate the relative reactivity of the thiocyanate group as a leaving group. As also shown in Table 1, the thiocyanate group was much less reactive than the bromide group but its reactivity was comparable to that of the chloride leaving group.

Instead of hexadecyltributylphosphonium azide, benzyltributylphosphonium azide was used for the substitution of benzyl thiocyanate in benzene. The reaction was slightly slower compared with HTBP azide but the reaction proceeded quantitatively to give benzyl azide as the only product. The rate constant, k_2, was 5.3×10^{-3} mol^{-1} dm^3 s^{-1}. Similarly, the reaction of benzyl thiocyanate with benzyltributylphosphonium chloride gave an equilibrium mixture of the corresponding products. The equilibrium constant (1.50) was almost same as with HTBPC.

Alkyl thiocyanates also undergo nucleophilic substitutions with halide ions. The reactivity of butyl thiocyanate with chloride ions was too poor to follow the reaction at 60 °C. With bromide or iodide ions, it took over 50 hours to attain the equilibrium in the reaction between butyl thiocyanate and HTBPX. HTBPB gave a larger equilibrium constant than HTBPI; K(Br) = 0.065 and K(I) = 0.0094. The magnitude of equilibrium constants was about 6 times larger than the values of the reactions with benzyl thiocyanate listed in Table 1. Decyl thiocyanate gave similar values of equilibrium constants for the reactions with bromide and iodide ions.

Effect of water and solvent on the displacement of thiocyanate

The addition of water significantly reduced the rate of the reactions, particularly slowing down the forward reaction due to an extensive hydration of the nucleophiles. An example of the reaction between benzyl thiocyanate and chloride ion is shown in Table 1 as well as in Fig. 4. The equilibrium constant also becomes small since k_{2-} does not change so much because of relatively weak hydration of the thiocyanate ions. The nucleophilicity of the azide ion was also reduced by the presence of water while no by-product was formed. As the rate of the nucleophilic substitution is suppressed by water, hydrazoic acid formed from azide and ammonium chloride in the presence of water may be responsible for the cycloaddition reported by the literature.[14]

Table 1 Reactions of benzyl thiocyanate with HTBPX in benzene-d$_6$ at 60 °C[a]

Substrate	X$^-$	w[b]	k_2 mol^{-1} dm^3 s^{-1}	k_{2-} mol^{-1} dm^3 s^{-1}	K
BnSCN	$(CH_3)_2NCS_2^-$	<0.1	0.67	—	—
	N_3^-	0.15	0.0157	—	—
	I$^-$	<0.1	0.00321	2.24	0.00143
	Br$^-$	<0.1	0.00126	0.114	0.0111
	Cl$^-$	0.37	0.000888	0.000621	1.43
		3.0	0.000072	0.000148	0.485
BnBr	N_3^-	0.15	1.56	—	—
BnCl	N_3^-	0.15	0.0405	—	—

[a] *Reactions conditions*: benzyl thiocyanate (BnSCN) was reacted with the hexadecyltributylphosphonium salt (HTBPX) in an NMR tube at 60 °C using 700 µL of benzene-d$_6$ as the solvent. To follow the reactions, the singlet methylene peaks were used as shown in the captions of Figs. 1 and 2. [b] The molar ratio of water to HTBPX.

The reaction between benzyl thiocyanate and quaternary salt was greatly influenced by solvent as summarized in Table 2. The rate of reaction between benzyl thiocyanate and azide ion was fast in benzene or in DMSO. In chloroform, the rate was relatively slow. This indicates that a solvent able to form hydrogen-bonds reduces the nucleophilic activity of anions as water does. A similar solvent effect was observed for the forward reaction of benzyl thiocyanate with chloride ion whereas solvent did not influence the rate of the reverse reaction so much. Thus, the equilibrium constant becomes small particularly in chloroform. The solvation due to the hydrogen-bonds is also important in methanol-d$_4$. Although the reverse reaction of benzyl chloride with thiocyanate ion is known to take place smoothly in alcohols (in fact, ethanol is often used as a solvent for the synthesis of alkyl thiocyanate from alkyl halide and thiocyanate salts), the forward reaction hardly proceeded in methanol as shown in Fig. 4. The solvation by methanol is responsible for this deceleration in the same manner. Furthermore, side reactions occur preferentially in methanol. A new singlet peak appeared at 4.15 ppm with a gradual decrease in benzyl thiocyanate (4.30 ppm) for the reactions with HTBPX. The singlet peak then decreased and several other peaks

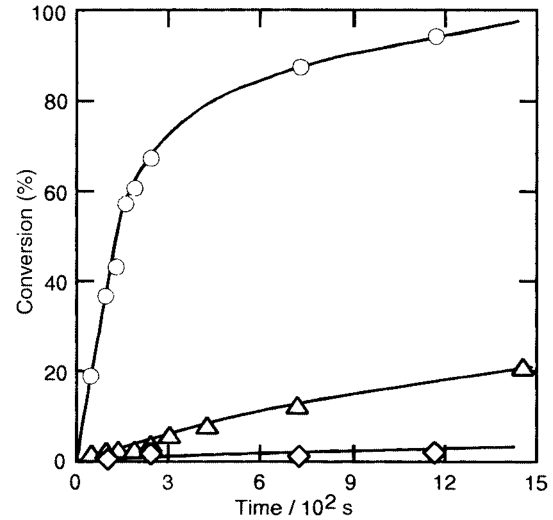

Fig. 4 Conversion plots for the reaction of benzyl thiocyanate with hexadecyltributylphosphonium chloride in benzene-d$_6$ or methanol-d$_4$ at 60 °C. *Reaction conditions*: 14 µmol of RSCN was allowed to react with 140 µmol of QX in an NMR tube at 60 °C using 700 µL of benzene-d$_6$ as solvent. In benzene, the molar ratio of water to HTBPC was 0.34 (○) or 12 (△). In methanol (◇). The singlet peak of benzyl thiocyanate appeared at δ_H 4.30 (PhCH_2SCN) in methanol.

Table 2 Solvent effect on the reactions of benzyl thiocyanate with HTBPX in deuteriated solvents at 60 °C[a,b]

X$^-$	Solvent	w[c]	k_2 mol^{-1} dm^3 s^{-1}	k_{2-} mol^{-1} dm^3 s^{-1}	K
N_3^-	Benzene-d$_6$	0.15	0.0157 (1.0)	—	—
	DMSO-d$_6$		0.0149 (0.9)	—	—
	Chloroform-d$_1$		0.00196 (0.1)	—	—
Cl$^-$	Benzene-d$_6$	0.37	0.000888 (1.0)	0.000621 (1.0)	1.43
	DMSO-d$_6$		0.00100 (1.1)	0.00133 (2.1)	0.752
	Chloroform-d$_1$		0.0000349 (0.04)	0.000667 (1.1)	0.0523

[a] *Reaction conditions*: benzyl thiocyanate (BnSCN) was reacted with hexadecyltributylphosphonium salt (HTBPX) in an NMR tube at 60 °C using 700 µL of deuteriated solvent. The peaks used to follow the reactions were the benzyl methylene peaks of the substrate and product: $\delta_H(C_6D_6)$ 3.39 (PhCH_2SCN), 3.80 (PhCH_2N$_3$), 4.18 (PhCH_2Cl); $\delta_H((CD_3)_2SO)$ 4.36 (PhCH_2SCN), 4.44 (PhCH_2N$_3$), 4.74 (PhCH_2Cl); $\delta_H(CDCl_3)$ 4.13 (PhCH_2SCN), 4.30 (PhCH_2N$_3$), 4.50 (PhCH_2Cl). [b] The numbers in parentheses represent the ratio of second-order rate constants in the solvent with respect to benzene. [c] The molar ratio of water to HTBPX.

Table 3 Reactions of benzyl thiocyanate with polymer-attached phosphonium salts at 60 °C[a,b]

X^- in Poly-X[c]	Solvent	k_2 / $mol^{-1}\,dm^3\,s^{-1}$
N_3^-	Benzene	0.0313 (1.0)
	Toluene	0.0346 (1.1)
	Tetrahydrofuran	0.0518 (1.6)
	Acetonitrile	0.0236 (0.8)
Cl^-	Benzene	0.00163
OAc^-	Benzene	0.00057

[a] *Reaction conditions*: 60 µmol of BnSCN was reacted with 60 µmol of nucleophiles at 60 °C using 2.0 mL of solvent. [b] The numbers in parentheses represent the ratio of second-order rate constants in the solvent with respect to benzene. [c] Poly-X: 200–400 mesh polystyrene resin with 1% divinylbenzene cross-linkage containing 0.8 mmol g^{-1} of nucleophile as counterion of the benzyltributylphosphonium salt.

Table 4 Reactions of decyl thiocyanate with aqueous potassium halides under two-phase or three-phase conditions at 90 °C[a]

KX	Catalyst[b]	Conversion of DcSCN at equilibrium state (%)
KBr	None	—
KBr	TOMAB	7.8
KBr	Poly-Br	4.3
KI	None	—
KI	TOMAI	18.7
KI	Poly-I	16.0

[a] *Reaction conditions*: 0.3 mmol of decyl thiocyanate in 2.0 mL of toluene was reacted with 6.0 mmol of KI or KBr in 2.0 mL of water at 90 °C in the presence of 50 µmol of quaternary salt. Conversions were analyzed by GLC. [b] TOMAX: tricotylmethylammonium halide (X = Br or I). Poly-Br, Poly-I; 200–400 mesh polystyrene resin with 1% divinylbenzene cross-linkage containing 0.8 mmol g^{-1} of benzyltributylphosphonium bromides or iodides.

appeared which we have not assigned. The singlet peak at 4.15 ppm was likely to be due to the benzyl methylene of benzyl isothiocyanate. In DMSO, the reaction of benzyl thiocyanate with HTBPX (X = halide) soon attained its chemical equilibrium. After that, with a very slow decrease in the singlet peak of benzyl thiocyanate at 4.36 ppm in DMSO, another singlet peak appeared and then disappeared at 4.50 ppm. Therefore, the rearrangement of benzyl thiocyanate to benzyl isothiocyanate is liable to take place in polar solvents with high relative permittivity.

Reactions of alkyl thiocyanate with polymer-attached phosphonium salts

Instead of soluble low-molecular phosphonium salts, polystyrene-attached phosphonium salts (Poly-X) were reacted with benzyl thiocyanate at 60 °C. The reactions were easily followed by GLC analysis of the solvent phase but the simple rate analysis according to eqn. (1) was slightly difficult because the material balance in the solvent phase was not necessarily good. As it is necessary to use a large amount of polymer reagents under stoichiometric reaction conditions, the different partition of benzyl thiocyanate and the product between solvent oil and the polymer resin phase probably causes this effect. Poly-N_3 selectively gave benzyl azide as the only product and the reaction proceeded irreversibly as with soluble hexadecyltributylphosphonium azide. The results are shown in Table 3, where we ignored the small deviation of the material balance to compute the rate constants or equilibrium constants. The second-order rate constant in benzene was slightly larger than that obtained for the soluble phosphonium salt. No large difference in rate constant was observed among the aprotic solvents used. The reaction in methanol was too slow to obtain the rate constant. The reactions with polymer-supported phosphonium halides gave the corresponding benzyl halides as the initial products. The material balances in the benzene phase were poor. Furthermore, the yield of benzyl bromide or iodide reached a maximum value and then gradually decreased owing to the minimal presence of the residual chloride ions in Poly-Br or Poly-I. The time–conversion curves at initial stages roughly suggested that the rate constants of the forward and reverse reactions with polymer-attached phosphonium halides had the same orders of magnitude as were observed for HTBPX. Table 3 only shows the rate constant for Poly-Cl. The apparent equilibrium constant was 1.58, which was close to that obtained for HTBPC. These results indicate the same chemical reactions take place as well with Poly-X.

Catalytic reactions of alkyl thiocyanates with inorganic nucleophiles

Decyl thiocyanate in toluene was allowed to react with aqueous KCl, KI, or KBr in the presence of a soluble ammonium salt or polystyrene-supported phosphonium salt at 90 °C. The reaction with aqueous KCl did not proceed for at least one day probably because chloride ions were highly hydrated under the conditions. For the reaction with aqueous KBr or KI, the corresponding alkyl halide was obtained. However, the reactions stopped at a particular conversion of decyl thiocyanate to give equilibrium mixtures. As shown in Table 4, the conversion at equilibrium was generally low even though a large excess of potassium halide was employed. The participation of ion exchange reaction (5) may cause these results. Since thiocyanate

$$KX + Q^+SCN^- \rightleftharpoons KSCN + Q^+X^- \qquad (5)$$

ions have a large affinity to quaternary ions, the equilibrium of reaction (5) tends to lie to the left. The amount of effective nucleophile has been lowered under these conditions. The equilibrium constant of the reaction with chloride ions may be additionally reduced by this effect. The use of solid KI instead of aqueous KI did not improve the yield of decyl iodide (about 10% yield).

Catalytic reactions between alkyl thiocyanate and alkyl halides

If reaction (4) is combined with the reaction (6), however, the

$$R'X + Q^+SCN^- \overset{K'}{\rightleftharpoons} R'SCN + Q^+X^- \qquad (6)$$

forward reaction of reaction (4) and the thiocyanation of alkyl halide (R′X) may proceed smoothly because the value of K' can be estimated to be close to the reciprocal value of K. As expected, the thiocyanation of butyl bromide with benzyl thiocyanate proceeded in the presence of a catalytic amount of HTBPB at 60 °C. However, the rate of reaction was very slow unless a large amount of the catalyst was applied. Thus, the reaction temperature was raised to 90 °C and polystyrene-supported phosphonium halide (Poly-X) was used as a catalyst instead of HTBPB. The progress of the reaction was followed by GLC. As shown in Fig. 5, the reaction of benzyl thiocyanate with butyl or decyl iodide proceeded at a reasonable rate to give an equilibrium mixture after 10 h. The conversions at equilibrium were about 70%, indicating that the over-all equilibrium constant was about 0.38. This means that K for benzyl thiocyanate is smaller than K for butyl or decyl thiocyanate. As already mentioned, however, benzyl thiocyanate is liable to rearrange to benzyl isothiocyanate. A prolonged reaction time over 10 h indeed induced the gradual formation of the by-product. This property of benzyl thiocyanate may make it inappropriate to use the compound as a thiocyanation reagent for synthetic purposes.

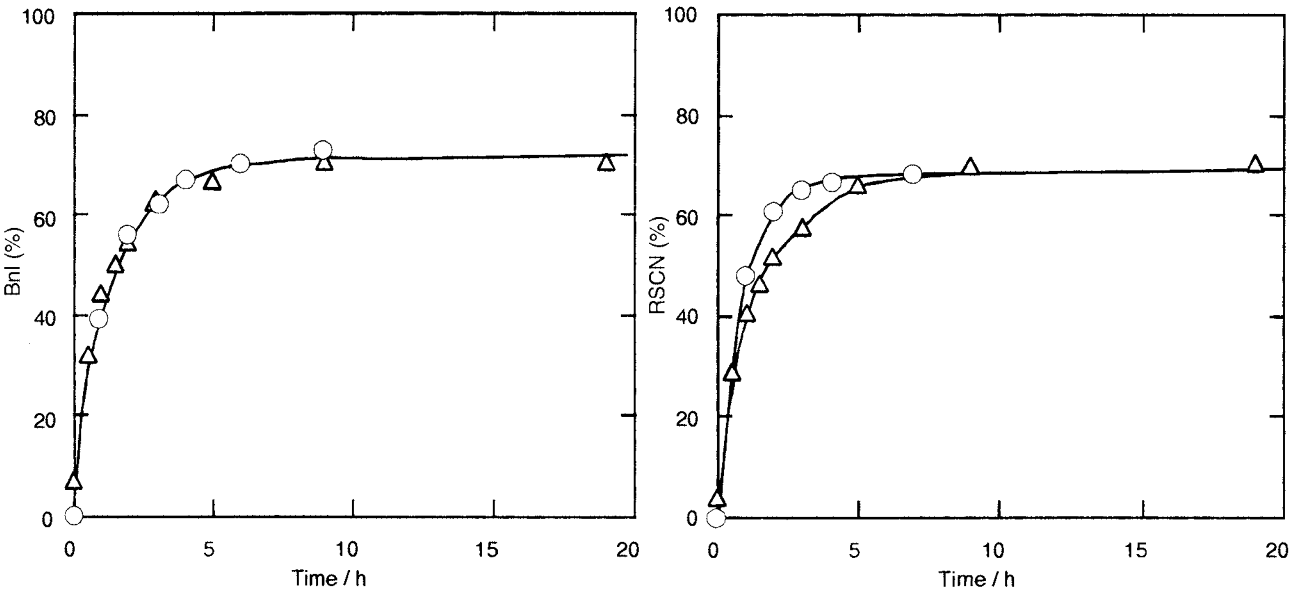

Fig. 5 Conversion plots for the reaction of decyl (△) or butyl (○) iodide with benzyl thiocyanate in toluene (2.0 mL) at 90 °C catalyzed by Poly-I (50 μmol).

Table 5 Reactions of methyl thiocyanate with alkyl halides catalysed by polymer-supported phosphonium halides at 90 °C[a]

RX	Catalyst	Solvent	Yield of RSCN[b]
BuI	Poly-I	Toluene	99
HpI	Poly-I	Toluene	90
BnBr	Poly-Br	Toluene	95[c]
BnI	Poly-I	Toluene	98[c]
OcBr	Poly-Br	Toluene	92
DcCl	Poly-Cl	Toluene	5.8
DcBr	Poly-Br	Toluene	98
DcI	Poly-I	Toluene	97
DcI	Poly-I	Octane	85
DcI	Poly-I	Chlorobenzene	90

[a] *Reaction conditions*: 0.2 mmol of alkyl halide and 1.0 mmol of methyl thiocyanate in 2.0 mL of solvent was reacted in the presence of 50 μmol of polystyrene-supported phosphonium salts (Poly-X: 12 percent ring substitution resin). [b] GLC yield after 12 h. [c] The maximum yield was found after around 8 h due to the rearrangement of the product when the reaction was left for longer.

Simple alkyl thiocyanates are more thermally stable. When methyl thiocyanate is used as a thiocyanation reagent, the volatility of the methyl halide, one of the products, facilitates the progress of the reaction. Table 5 shows some typical examples of this synthetic method. Each thiocyanate was formed in a good yield unless alkyl chloride was used. The solvent effect was also investigated. The initial rate was fastest in octane but the final yield was relatively low. An enhanced nucleophilicity of anions may be the primary reason for the fast reaction at the initial stage although other factors may affect the final yield of the present system such as relative affinity of the organic substances for the polymer catalyst and liquid phase. Nevertheless, the reaction with methyl thiocyanate could be used as a novel method for the synthesis of an alkyl thiocyanate. This thiocyanation method may be useful for the synthesis of such an alkyl thiocyanate when anhydrous conditions are absolutely necessary in the preparation.

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