

Isomerization Mechanism of α -Phenethyl Thiocyanate in the Presence of a Supported Reagent

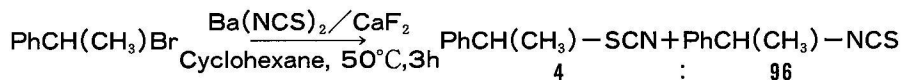
Takahide Kimura, Mitsue Fujita, Hajime Sohmiya, and Takashi Ando
Department of Chemistry, Shiga University of Medical Science, Otsu, Shiga 520-21

Received March 8, 1995

The isomerization of α -phenethyl thiocyanate to the corresponding isothiocyanate was observed in the course of the isothiocyanation reaction of α -phenethyl bromide with $\text{Ba}(\text{NCS})_2$ supported on CaF_2 in cyclohexane. The most probable reaction mechanism is suggested as an SN_2 -like push-pull mechanism with the assistance of α -phenethyl bromide and $\text{BaBr}_2/\text{CaF}_2$.

Interest in using supported reagents for organic synthesis has developed tremendously because of easy product isolation, mild reaction conditions, and rapid and selective course of reaction. We recently reported the dramatic change in the sulfur - nitrogen selectivity of the SCN substitution of *t*-butyl bromide by simply supporting various alkaline earth metal thiocyanates on various inorganic solids.¹ For example, $\text{Ba}(\text{NCS})_2$ supported on CaF_2 with *t*-butyl bromide gave a 79% yield of a mixture of *t*-butyl thiocyanate and isothiocyanate in the ratio of 1 : 99 in cyclohexane after 3 h at 50°C, while $\text{Ba}(\text{NCS})_2$ supported on BaF_2 gave a 26% yield of the products in the ratio of 82 : 18 under the same conditions. The solid supports have the dramatic effect not only on the reactivity but also on the selectivity, therefore salt - support interactions must be important in changing the relative nucleophilicity of the S and N atoms of the SCN^- anion.

During the extension of this study, summarized in Table 1, we observed an isomerization of products, α -phenethyl thiocyanate and isothiocyanate in the reaction of α -phenethyl bromide with $\text{Ba}(\text{NCS})_2$ supported on CaF_2 ($\text{Ba}(\text{NCS})_2/\text{CaF}_2$).



$\text{Ba}(\text{NCS})_2/\text{CaF}_2$ gave a 61% yield of a mixture of α -phenethyl thiocyanate and isothiocyanate in the ratio of 4 : 96 under the same conditions as for the reaction of *t*-butyl bromide, while unsupported $\text{Ba}(\text{NCS})_2$ gave a 14% yield in the ratio of 93 : 7. Although the isomer ratio obtained with $\text{Ba}(\text{NCS})_2/\text{CaF}_2$ was similar for α -phenethyl bromide and *t*-butyl bromide, a distinct difference appeared in the course of the reaction, as shown in Figs. 1a and b. In the reaction of *t*-butyl bromide with $\text{Ba}(\text{NCS})_2/\text{CaF}_2$, the formation of *t*-butyl isothiocyanate is a result of the kinetic control, and there is minimal isomerization

Table 1. Reaction of Alkyl Halide with unsupported $\text{Ba}(\text{NCS})_2$ and $\text{Ba}(\text{NCS})_2$ supported on CaF_2 ^{a)}

Substrate	Reagent ^{b)}	GC Yield (%)	Products	
			Isomer ratio ^{c)}	
			Thiocyanate : Isothiocyanate	
t-Bu-Br	a	6	91 : 9	
	b	79	1 : 99	
PhCH(CH ₃)-Br	a	14	93 : 7	
	b	61	4 : 96	
1-Adamantyl-Br ^{d)}	a	4	78 : 22	
	b	49	82 : 18	
PhCH ₂ -Br	a	22	100 : 0	
	b	48	100 : 0	
PhCH=CHCH ₂ -Cl	a	91	43 : 57	
	b	90	79 : 21	

a) Alkyl halide and $\text{Ba}(\text{NCS})_2$, each of 0.5 mmol. Cyclohexane as a solvent (5 mL) Reaction time and temperature, 3 h and 50°C, respectively. b) Reagent a: unsupported $\text{Ba}(\text{NCS})_2$; reagent b: $\text{Ba}(\text{NCS})_2$ (0.5 mmol) supported on CaF_2 (1 g). c) Determined by GC. d) Reaction time, 20 h.

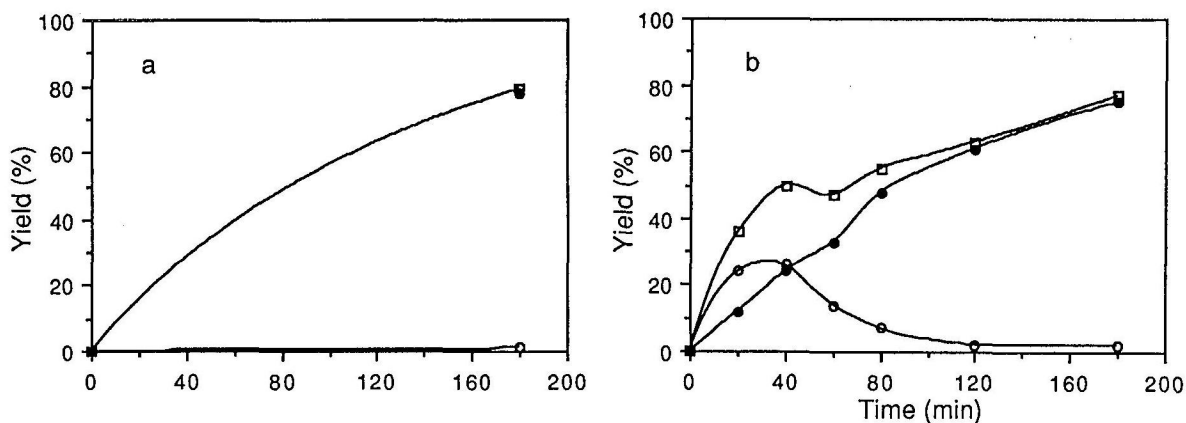


Figure 1. Time dependent profile of the production of thiocyanate (○) and isothiocyanate (●) in the reaction of (a) t-butyl bromide and (b) α -phenethyl bromide with $\text{Ba}(\text{NCS})_2$ supported on CaF_2 . (Total yield: □) Alkyl bromide 0.5 mmol; $\text{Ba}(\text{NCS})_2/\text{CaF}_2$ 0.5 mmol/g; cyclohexane (5 mL) as a solvent at 50°C.

of t-butyl thiocyanate to t-butyl isothiocyanate, which is thermally more stable than thiocyanate. For α -phenethyl bromide, on the other hand, the system first proceeds toward the formation of the kinetic product, thiocyanate. This derivative appears only at the beginning of the reaction, allowing the isothiocyanate isomer, a thermodynamic prod-

uct, to accumulate.

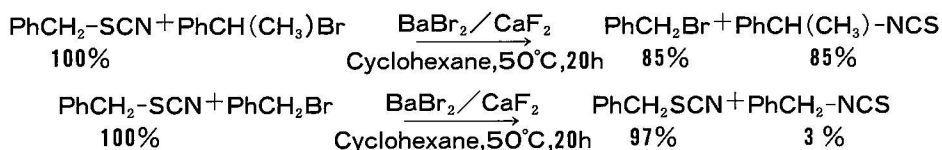
Isomerization of *t*-butyl thiocyanate and α -phenethyl thiocyanate to the corresponding isothiocyanates was not catalyzed by the supported reagent, $\text{Ba}(\text{NCS})_2/\text{CaF}_2$. Other materials that catalyze the isomerization of α -phenethyl thiocyanate must be present in the reaction medium. Therefore, the catalytic ability of materials that might be present in the reaction medium were examined for the isomerization. The results are illustrated in Fig. 2. When a mixture of α -phenethyl thiocyanate and isothiocyanate was heated at 50°C for 20 h in cyclohexane in the presence of CaF_2 , BaBr_2 , α -phenethyl bromide, $\text{Ba}(\text{NCS})_2/\text{CaF}_2$, $(\text{CaF}_2 \text{ plus } \text{BaBr}_2)$, or $(\alpha\text{-phenethyl bromide plus } \text{BaBr}_2)$, the isomer ratio of the mixture was almost unchanged. On the other hand, $\text{BaBr}_2/\text{CaF}_2$, $(\alpha\text{-phenethyl bromide plus } \text{CaF}_2)$, or $(\alpha\text{-phenethyl bromide plus } \text{BaBr}_2/\text{CaF}_2)$ catalyzed the isomerization. Particularly, the isomerization was very fast in the presence of both α -phenethyl bromide and $\text{BaBr}_2/\text{CaF}_2$.

Obviously, interaction between CaF_2 and Br of α -phenethyl bromide and/or BaBr_2 is important for the occurrence of the isomerization.

Several investigations have reported on the isomerization of alkyl thiocyanates to the corresponding isothiocyanates.²⁻⁴ It is known that *t*-butyl bromide reacts with $\text{Hg}(\text{SCN})_2$ to give *t*-butyl isothiocyanate, but that *t*-butyl thiocyanate does not isomerize to *t*-butyl isothiocyanate with $\text{Hg}(\text{SCN})_2$ or HgBr_2 .² Nevertheless, we found that *t*-butyl thiocyanate does isomerize in the presence of both HgBr_2 and *t*-butyl bromide under the present reaction conditions; the ratio of thiocyanate and isothiocyanate changed from 81 : 19 to 27 : 73 in 2 h in cyclohexane at 50°C .

The isomerization of α -phenethyl thiocyanate to the corresponding isothiocyanate occurred readily in the system composed of KSCN in DMF.² This is natural, as the free SCN^- ion should be formed in the dipolar aprotic solvent and an SN_1 mechanism occurs. In a non-polar solvent, however, it is difficult to postulate the SN_1 -like mechanism, that is, an alkyl thiocyanate dissociates to a carbocation and a thiocyanate ion, and recombines to give a thermodynamically stable alkyl isothiocyanate. The acceleration of the isomerization by α -phenethyl bromide strongly suggests that a push-pull process which involves the push by $^\delta\text{-NCS}\cdots\text{R}^\delta+\cdots\text{Br}-\text{Ba}-\text{Br}-\text{CaF}_2$ and the pull by $\text{R}^\delta+\cdots\text{Br}^\delta-\cdots\text{BaBr}_2-\text{CaF}_2$ may operate. In a similar reaction of alkyl halides with silver nitrate, the contribution of a push-pull mechanism has already been established.³

In order to study the interaction of alkyl bromide with alkyl thiocyanate, the isomerization of benzyl thiocyanate was followed in the presence of α -phenethyl bromide and $\text{BaBr}_2/\text{CaF}_2$ or of benzyl bromide and $\text{BaBr}_2/\text{CaF}_2$.



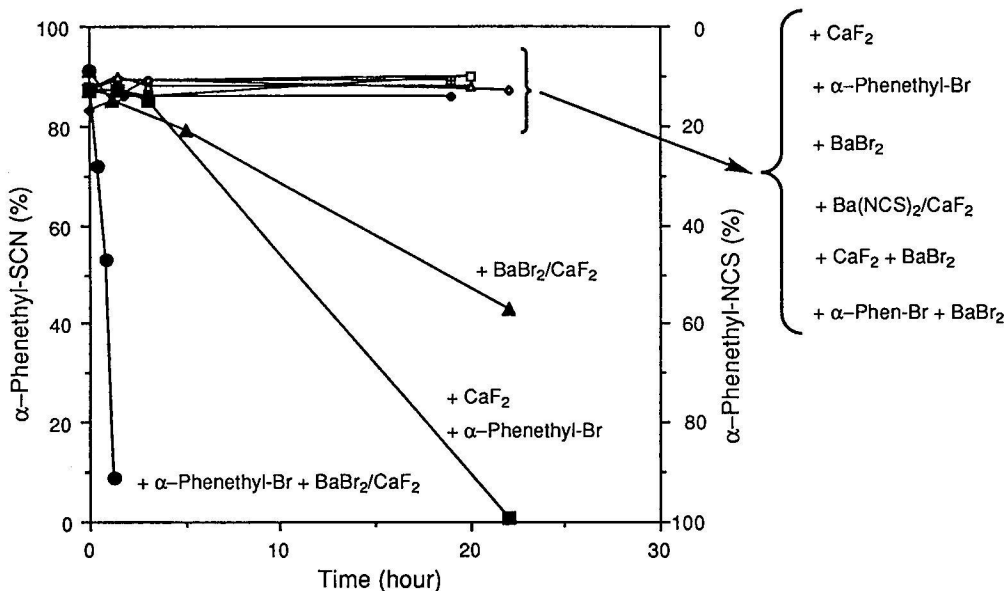
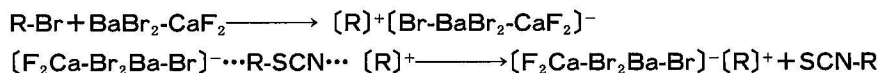


Figure 2. Catalytic abilities of various materials to isomerize α -phenethyl thiocyanate. A mixture of α -phenethyl thiocyanate and isothiocyanate 0.5 mmol; catalysts: α -phenethyl bromide, $\text{Ba}(\text{NCS})_2$, and BaBr_2 , each of 0.5 mmol or CaF_2 1g; cyclohexane (5 mL) as a solvent at 50°C .

Only α -phenethyl bromide was substituted with SCN of benzyl thiocyanate to give α -phenethyl isothiocyanate, while benzyl bromide seemed to be unchanged. Thus, it is reasonable that Br of secondary alkyl bromide is pulled by $\text{BaBr}_2/\text{CaF}_2$ to a greater extent than Br of primary alkyl bromide, making it more carbocationic in character. In a non-polar solvent, the nature of the substitution reaction should still be $\text{S}_{\text{N}}2$ -like. Therefore, *t*-butyl thiocyanate and 1-adamantyl thiocyanate did not isomerize as presented in Table 1 because of their steric hindrance. A presumed mechanism for the isomerization of α -phenethyl thiocyanate in the presence of $\text{BaBr}_2/\text{CaF}_2$ and α -phenethyl bromide can be summarized in the following scheme.



REFERENCES

1. T. Kimura, M. Fujita, and T. Ando, *J. Chem. Soc., Chem. Commun.*, 1213 (1990).
2. a) A. Iliceto, A. Fava, U. Mazzucato, and O. Rosseto, *J. Am. Chem. Soc.*, **83**, 2729 (1961); b) A. Fava, A. Iliceto, and S. Bresadola, *J. Am. Chem. Soc.*, **87**, 4791 (1965); c) A. Ceccon, A. Fava, and I. Papa, *J. Am. Chem. Soc.*, **91**, 5547 (1969).

3. N. Watanabe, M. Okano, and S. Uemura, *Bull. Chem. Soc. Jpn.*, **47**, 2745, (1974).
4. R. Catusse, R. El Gharbi, and A. Gaset, *Reactive Polymers*, **8**, 79 (1988).
5. N. Kornblum, R. A. Smiley, R. K. Blackwood, and D. C. Iffland, *J. Am. Chem. Soc.*, **77**, 6269 (1955).