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Support-controlled Switching of Sulphur–Nitrogen Nucleophilicity for Inorganic Solid-supported Alkaline Earth Metal Thiocyanate Reagents

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A dramatic change in the sulphur–nitrogen selectivity of the SCN substitution of t-butyl bromide was observed, in addition to a dramatic increase in reaction rate, by simply supporting various alkaline earth metal thiocyanates on various inorganic solids.

Interest in using supported reagents for convenient, rapid, and selective organic synthesis has grown tremendously during the last ten years.¹ We recently showed that the reactivity of potassium thiocyanate was greatly improved for substitution of various primary, secondary, and tertiary alkyl halides by optimizing the salt–support interaction.² Although isothiocyanates, formed by nucleophilic attack of the harder nitrogen end of the SCN[−] anion, were increasingly obtained as the S_N1 character of the substitution increased, the selectivity was never excellent. Previous studies have shown that the S–N nucleophilicity can be greatly influenced by the counter-metal ion, mercury(II) and copper(II) thiocyanates favouring attack by nitrogen.³ During a study on the effects of alkaline earth metal cations of thiocyanate salts and various inorganic solid-supports in the SCN substitution of t-butyl bromide, we found that the S–N nucleophilicity of alkaline earth metal thiocyanates was finely balanced and controllable.

For example, unsupported Ba(NCS)₂[†] with t-butyl bromide gave a 6% yield of a mixture of t-butyl thiocyanate and isothiocyanate in cyclohexane after 3 h at 50 °C. The thiocyanate vs. isothiocyanate ratio (S:N) was 91:9 (Table 1).

When Ba(NCS)₂ (0.5 mmol) was impregnated on CaF₂ (1 g),[‡] the yield became 79% under the same conditions as with unsupported reagent and the product ratio was found to be 1:99, *i.e.*, the main product was t-butyl isothiocyanate.[‡] Although alkyl isothiocyanates are thermally more stable than thiocyanates, it was found that the supported reagents did not

catalyse the isomerization. Therefore the formation of t-butyl isothiocyanate by Ba(NCS)₂–CaF₂ is not a result of thermodynamic control, but of kinetic control. On the other hand, when Ba(NCS)₂ (0.5 mmol) impregnated on CaCO₃ (1 g) was used, the yield was 57% and the product ratio was 95:5. The change of supports from CaCO₃ to CaF₂ changed the selectivity 1900 fold. Other alkaline earth metal fluorides, SrF₂ and BaF₂, used as supports gave mixtures of the thiocyanate and isothiocyanate in varying ratios. Thus, the solid supports have a dramatic effect not only on the reactivity but also on the selectivity. As the size of the metal ions of the fluoride supports becomes smaller and the electron density becomes larger, the yield of the isothiocyanate increases.

A similar tendency was observed for Sr(NCS)₂, but the opposite results were found for Ca(NCS)₂. In the latter case BaF₂ as a support gave 89% selectivity for isothiocyanate formation, but CaF₂ 17%. Obviously, salt–support interactions are important in changing the relative nucleophilicity of the S and N atoms of the SCN[−] anion. In order to study the

Table 1. Reactivity and selectivity of nucleophilic substitutions of t-butyl bromide with supported and unsupported various alkaline earth metal thiocyanates.[‡]

M(NCS) ₂	Support	Yield (%)	S:N	$\nu_{\text{SCN}}/\text{cm}^{-1}$
Ba(NCS) ₂	—	6	91:9	2086
	CaCO ₃	57	95:5	2087
	BaF ₂	26	82:18	2072
	SrF ₂	8	41:59	2068
	CaF ₂	79	1:99	2063
Sr(NCS) ₂	—	4	94:6	2071
	BaF ₂	48	65:35	2065, 2099
	SrF ₂	11	83:17	2065, 2103
	CaF ₂	64	35:65	2065
Ca(NCS) ₂	—	19	95:5	2073
	BaF ₂	36	11:89	2064
	SrF ₂	45	93:7	2090
	CaF ₂	100	83:17	2071

[†] Unsupported Ba(NCS)₂ was dried at 50 °C and 0.1 mmHg for 17 h before use. Supported Ba(NCS)₂ was prepared as follows: Ba(NCS)₂·2H₂O (5 mmol) was dissolved in water (100 ml), then the inorganic supporting material (10 g) was added. The water was removed by using a rotary evaporator at 50 °C. The resulting solid was dried at 50 °C and 0.1 mmHg for 17 h.

[‡] Typical reactions were carried out as follows. To t-butyl bromide (0.5 mmol) in cyclohexane (5 ml) containing biphenyl as a GC standard, the supported Ba(NCS)₂ (1 g, 0.5 mmol) was added. The mixture was then shaken in a screw-capped test tube at 50 °C for 3 h. Yields of t-butyl thiocyanate and isothiocyanate were determined by GC analysis.

distribution of electron density in the thiocyanate ion, IR spectra were taken of the supported and unsupported reagents. § The asymmetric SCN⁻ stretching absorption of Ba(NCS)₂ itself is at 2086 cm⁻¹, that of Ba(NCS)₂-CaF₂ at 2063 cm⁻¹, and that of Ba(NCS)₂-CaCO₃ at 2087 cm⁻¹. Ca(NCS)₂ itself has an absorption at 2073 cm⁻¹, and Ca(NCS)₂-BaF₂ at 2064 cm⁻¹. As the S-N selectivity and IR spectra are similar for Ba(NCS)₂-CaF₂ and Ca(NCS)₂-BaF₂, the same reacting species may be produced on the surface of the supported reagents. According to the literature⁴ the NCS group is co-ordinated to barium *via* nitrogen. Thus, it is reasonable that the more sterically favourable and more electronegative S end preferentially attacks the carbocationic centre of *t*-butyl bromide. On the other hand the IR data of Ba(NCS)₂-CaF₂ and Ca(NCS)₂-BaF₂ seem to indicate that the NCS group is less strongly bonded to the metal ion, that is, the ionic character of the NCS group is increased. Therefore, the harder N end is 'free' to attack the hard carbocationic centre. In the case of CaCO₃, the oxygen atoms of the CO₃²⁻

§ IR spectra were obtained on a Perkin-Elmer FT-IR spectrometer 1720 for Nujol mulls.

group may form a different and more complex interaction with metals.

In summary, our findings on the SCN substitution of *t*-butyl bromide clearly show that the interaction between solid reagents and solid supports is decisively important for not only the reactivity but also the selectivity of inorganic solid-supported reagents.

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References

- 1 'Preparative Chemistry Using Supported Reagents,' ed. P. Laszlo, Academic Press, London, 1987.
- 2 T. Ando, J. H. Clark, D. G. Cork, M. Fujita, and T. Kimura, *J. Org. Chem.*, 1987, **52**, 681.
- 3 N. Watanabe, M. Okano, and S. Uemura, *Bull. Chem. Soc. Jpn.*, 1974, **47**, 2745.
- 4 'Chemistry of Pseudohalides,' eds. A. M. Golub, H. Köhler, and V. V. Skopenko, Elsevier, Amsterdam, 1986, ch. 5.