Selective Formation of Isonitriles by Anodic Oxidation of α -Heteroatom-substituted Organotin Compounds

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Anodic oxidation of α -heteroatom-substituted organotin compounds in Bu₄NBF₄-THF results in the cleavage of the carbon-tin bond and exclusive formation of isonitriles whereas the reaction in Bu₄NClO₄-CH₂Cl₂ gives rise to exclusive formation of the corresponding nitriles.

The ambident character of trimethylsilyl cyanide (TMSCN), which exists as an equilibrium mixture of the nitrile form and the isonitrile form, has attracted considerable attention.¹ Although both nitrile formation and isonitrile formation have been known for the Lewis acid catalysed reaction with organic halides² and epoxides,³ only cyanide formation has been reported for the reaction with carbonyl compounds⁴ and acetals⁵ [Scheme 1(*a*) and (*b*)]. Pioneering work by Reetz and coworkers suggested that initially formed α -heteroatom-substituted isonitriles isomerize to nitriles by the catalysis of Lewis acid, but there is no direct evidence for the formation of α -heteroatom-substituted isonitriles.^{5b†} Presumably, α -heteroatom-substituted isonitriles are extremely unstable under the conditions and isomerize spontaneously to the nitriles.

Recently, we have found that α -heteroatom-substituted carbocations can also be generated by an electrochemical method. Although organotin compounds are efficient precursors of carbanions by using transmetallation reactions,⁶ the anodic oxidation of α -heteroatom-substituted organotin compounds results in the facile cleavage of the carbon-tin bond and the introduction of nucleophiles such as alcohols,



allylsilanes, and silyl enol ethers onto the carbon.^{7,8} Since the electrochemical oxidation can be carried out under neutral conditions by choosing appropriate reaction conditions, we were interested in the reaction of electrochemically generated carbocations with TMSCN. Herein, we report that anodic oxidation of α -heteroatom-substituted carbocations in the presence of TMSCN leads to selective formation of isonitriles without isomerization to nitriles under certain conditions [Scheme 1(c)].

Anodic oxidation of α -alkoxy organotin compounds in the presence of TMSCN in an undivided cell equipped with a carbon-rod anode and a platinum plate cathode in Bu₄NBF₄-THF resulted in selective formation of the corresponding isonitrile (Table 1). The effects of the solvent and the supporting electrolyte are significant. Switching of the solvent to CH₂Cl₂ gave rise to the formation of a mixture of the isonitrile and the nitrile, although they were easily separated by flash chromatography. The anodic oxidation in Bu_4NCIO_4- CH₂Cl₂ afforded the nitrile as the major product. The nitrile was obtained selectively when excess amount of electricity was passed. Tin-substituted sulfides and carbamates were also effective as α -heteroatom-substituted organotin compounds. Although in the case of tin-substituted carbamates a significant amount of nitrile was formed even in Bu₄NBF₄-THF, the addition of 2,6-lutidine raised the ratio of isonitrile : nitrile up to 85:15.

As to the reaction mechanism the following explanation seems to be reasonable (Scheme 2). One-electron oxidation of the organotin compound followed by the homolytic cleavage‡ of the carbon-tin bond produces the carbocation intermediate stabilized by the heteroatom. TMSCN attacks the carbocation at nitrogen to afford the isonitrile. This is consistent with the fact that the equilibrium between TMSCN and TMSNC lies far on the left side.

The nitrile seems to be formed by electrogenerated acid (EGA)-catalysed isomerization of the initially formed isonitrile.⁹§ In THF such isomerization is retarded presumably because THF is more basic than CH_2Cl_2 and therefore neutralizes the EGA. When ClO_4^- is used as the supporting electrolyte, the rection medium becomes more acidic and therefore the isomerization seems to be accelerated. When the reaction was carried out in Bu_4NClO_4 - CH_2Cl_2 in the presence of a base such as 2,6-lutidine, the significant amount of the isomitrile was obtained, indicating that the base retarded the isomerization.

The isomerization of menthyloxymethyl isonitrile to the corresponding nitrile was examined with several acid catalysts. With Lewis acids shown in Scheme 3, the isomerization completed in 5 min at room temp. It should be noted that even ZnI₂ and SnCl₂ which catalyse the selective isocyanation of epoxides also catalysed the isomerization, indicating that α -heteroatom-substituted isonitriles are highly sensitive to acids. Therefore, if α -heteroatom-substituted isonitriles are formed in Lewis acid catalysed reactions with TMSCN, they isomerize almost spontaneously to the nitriles. EGA produced by the electrolysis of Bu₄NClO₄ or Bu₄NBF₄-CH₂Cl₂ also catalysed the isomerization.

The present study demonstrates the effectiveness of the electrochemical oxidation of organotin compounds as an

Table 1 Anodic oxidation α -heteroatom-substituted organotin compounds in the presence of trimethylsilyl cyanide^a

Organotin compound	Solvent	electrolyte	Charge/F	Products ^b	Yield (%)
on Subus	THF	Bu ₄ NBF ₄	2.6		84 CN
	CH ₂ Cl ₂	Bu₄NBF₄	2.2	83:17	84
	CH2CP	Bu ₄ NClO ₄	2.2	13:87	85
	CH ₂ Cl ₂	Bu ₄ NClO ₄	3.3	0:100 ⁷	82
OMe C7H15 SnBu₃	THF	Bu ₄ NBF ₄	2.2	OMe OMe C7H15 NC C7H15 CN 100:0 ^d	52
	CH ₂ Cl ₂	Bu ₄ NCIO ₄	3.0	0:100°	64
SPh CgH₁7 SnBu₃	THF	Bu ₄ NBF ₄	2.4	SPh SPh C ₈ H ₁₇ NC C ₈ H ₁₇ CN 100:0 ^d	53
	CH ₂ Cl ₂	Bu ₄ NCIO ₄	2.2	10: 9 0	68
	CH ₂ Cl ₂	Bu ₄ NClO ₄	3.0	0:100 [●]	69
	CH ₂ Cl ₂ ¹	Bu ₄ NCIO ₄	5.0	51:49	62
CO₂Me C12H25∽N∽SnBu3	THF	Bu ₄ NBF ₄	2.2	C0₂Me C0₂Me C12H25 ^{-N} NC C12H25 ^{-N} CN 57:43	65
	THF ^g	Bu ₄ NBF ₄	3.0	85:15	64
	CH ₂ Cl ₂	Bu ₄ NClO ₄	2.0	0:100 [•]	91

^{*a*} Reactions were normally carried out under constant current conditions in an undivided cell equipped with a carbon rod anode and a platinum plate cathode using 0.2 mol dm⁻³ solution of Bu_4NBF_4 or Bu_4NClO_4 (1.0 ml) in the presence of molecular sieves 4 Å. ^{*b*} The ratio was determined by ¹H NMR. ^c The yield of the isolated mixture of isonitrile and nitrile. ^{*d*} No nitrile was observed by ¹H NMR. ^c No isonitrile was observed by ¹H NMR. ^f 2,6-Lutidine (1 equiv.) was added. ^g 2,6-Lutidine (3 equiv.) was added.

extremely mild method for generation of carbocations adjacent to a heteroatom.¹¹ Isonitriles can be obtained without isomerization using an appropriate supporting electrolyte/ solvent system. The present observations also suggest a general tendency of TMSCN to attack carbocations selectively at the N terminal forming isonitriles which isomerize almost spontaneously to the nitriles under the catalysis of Lewis acids. This tendency provides an interesting mechanistic implication to diastereoselective cyanation of optically active cyclic acetals¹² and enantioselective cyanosilylation of carbonyl compounds.¹³ The stereochemistry might be determined at the stage of isomerization of the initially formed isonitriles to nitriles, or both the isocyanation and the isomerization might be stereospecific.

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Footnotes

† Evidence for Lewis acid catalysed isomerization of isonitriles derived from alkyl halides to the nitriles has been reported.^{2a}

[‡] Homolytic cleavage of the C-Sn bond to produce the carbocation and Bu₃Sn has also been suggested by Narasaka *et al.* who oxidized α heteroatom-substituted organotin compounds by chemical oxidants such as CAN (personal communication). But a mechanism involving heterolytic cleavage to form the carbon radical which is further oxidized by anodic reaction may also be possible.

§ PM3 calculations¹⁰ indicated that MeOCH₂CN is 26.7 kcal mol⁻¹ more stable than MeOCH₂NC.

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J. CHEM. SOC., CHEM. COMMUN., 1994

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