

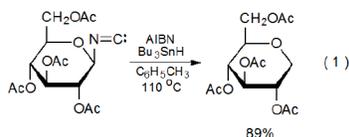
II. Isonitriles

A. Reactions

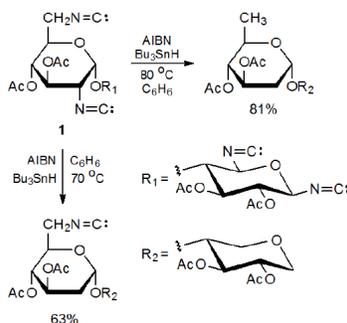
1. Group Replacement

a. Isocyano Groups

Reaction of tri-*n*-butyltin hydride with carbohydrates containing isocyano groups replaces each of these groups with a hydrogen atom. Such replacement is known to occur when isocyano groups are attached to anomeric,^{1,2} secondary,³⁻⁹ and primary⁷⁻⁹ carbon atoms. An example of replacement at an anomeric carbon atom is shown in eq 1,⁵ while both primary and secondary groups are replaced in the reaction described in Scheme 1.^{7,9}



Scheme 1

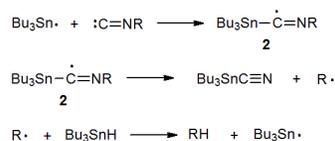


Isocyano group replacement is remarkably temperature sensitive. Reaction of the secondary groups in **1** takes place at 70 °C, but the primary isocyano group is unreactive (Scheme 1).^{7,9} When the temperature of the reaction mixture is raised to 80 °C, both groups are replaced. This temperature dependence provides a basis for regioselective reaction.

A mechanism for isocyano group replacement with a hydrogen atom is pictured in Scheme 2.¹⁰ In the first step of this process the tri-*n*-butyltin radical adds to the carbon atom of the isocyano group to produce an imidoyl radical (**2**). Fragmentation of this radical (**2**) then generates the carbon-centered radical R \cdot , which abstracts a hydrogen atom from Bu₃SnH to complete the reaction sequence. If R represents a phenyl or substituted-phenyl group, fragmentation to give an aryl radical does not occur; rather, an addition reaction takes place.¹¹ When tris(trimethylsilyl)silane replaces tri-*n*-butyltin hydride in reduction of isonitriles, compounds containing primary, secondary, or tertiary isocyano groups all are reactive.¹²

Scheme 2

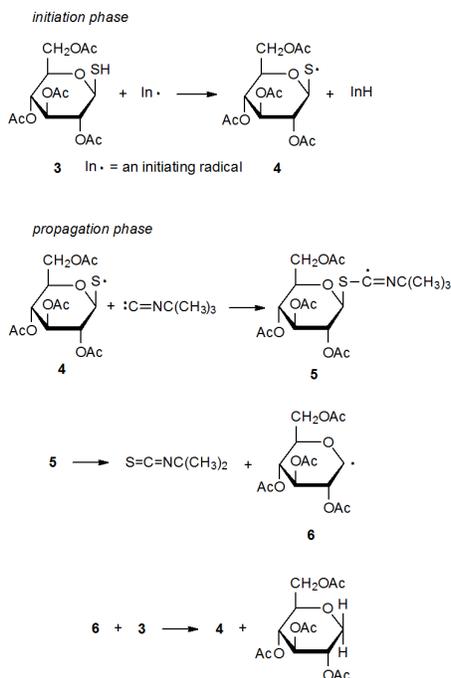
propagation steps



b. Sulfhydryl Groups

An isonitrile can participate in replacement of a sulfhydryl group by a hydrogen atom.¹³ Such a reaction is pictured in Scheme 3, where replacement begins when the sulfur-centered radical **4** forms from the thiol **3** by hydrogen-atom abstraction. Addition of **4** to *t*-butyl isocyanide gives the adduct radical **5**, which then fragments to produce the pyranos-1-yl radical **6**. Hydrogen-atom abstraction by **6** from another molecule of the starting thiol (**3**) completes the cycle and begins a new reaction sequence. Sulfhydryl group replacement represents another pathway for generating carbon-centered, carbohydrate radicals.

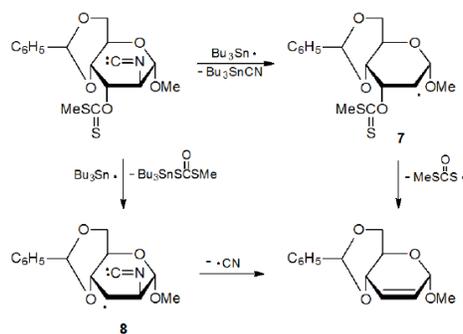
Scheme 3



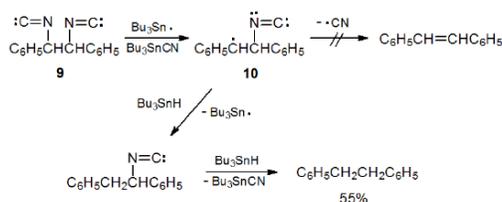
2. Elimination Reactions

Reaction of tri-*n*-butyltin hydride with a carbohydrate that has adjacent isocyano and *O*-thiocarbonyl groups generates a product with a C–C double bond (Scheme 4).⁴ In this reaction radicals **7** and **8** are both possible intermediates. Study of the diisocyanide **9** provides information helpful in choosing between **7** and **8**. Reaction of **9** with $\text{Bu}_3\text{Sn}\cdot$ produces a carbon-centered radical (**10**) with an isocyano group attached to the carbon atom adjacent to the radical center (Scheme 5).⁸ The intermediate **10** does not expel a cyano radical to form a multiple bond but rather abstracts a hydrogen atom from tri-*n*-butyltin hydride. Extrapolating the behavior of **10** to the reaction shown in Scheme 4 leads to the conclusion that the radical **8** is an unlikely intermediate in this process.

Scheme 4

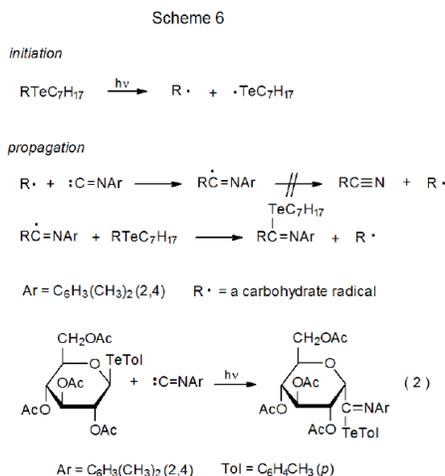


Scheme 5



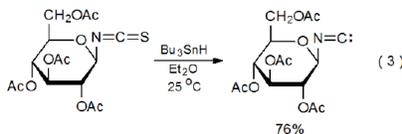
3. Addition Reactions

As a part of the replacement process shown in Scheme 2, an isonitrile reacts with $\text{Bu}_3\text{Sn}\cdot$ to produce an intermediate, carbon-centered radical $\text{R}\cdot$. Normal completion of this reaction involves hydrogen-atom abstraction by $\text{R}\cdot$ from Bu_3SnH ; however, if $\text{R}\cdot$ is formed without a hydrogen-atom transfer present, it will add to a molecule of isonitrile (Scheme 6). A specific example of this type of reaction is found in eq 2, which describes the α addition of a pyranos-1-yl radical, formed from a carbohydrate telluride, to an aromatic isonitrile.¹⁴

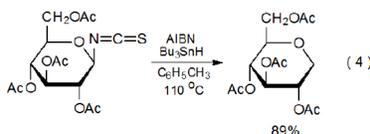
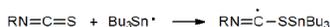


B. Synthesis

It is possible to produce isonitriles from isothiocyanates by radical reaction (eq 3).² A proposed mechanism for such a structural change is shown in Scheme 7. Isonitrile formation results when reaction is conducted at room temperature (eq 3), but if the reaction temperature is raised to 110 °C, the isonitrile is not isolated because it undergoes isocyno group replacement by a hydrogen atom (eq 4).^{2,15}



Scheme 7



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