Most mechanistic understanding of radical formation by dehalogenation comes from study of alkyl halides. It is reasonable to assume that the findings from these investigations also are applicable to reactions of halogenated carbohydrates but, at the same time, to recognize that such application does involve extrapolation of the data to more complex structures.

A. Evidence for Radical Intermediates

The radical nature of alkyl halide reaction with organotin hydrides first was proposed in a series of papers that began to appear in the early 1960s.\textsuperscript{3–7} One experiment that was part of this research concerned reaction of the optically active chloride 1 with (C\textsubscript{6}H\textsubscript{5})\textsubscript{3}SnD to form a racemic mixture of products. This result was consistent with a radical intermediate (2) participating in the reaction, but it also could be explained by the intermediacy of a carbocation (Scheme 2).\textsuperscript{3} (The proposed radical intermediate pictured in Scheme 2 as a planar structure also could be the rapidly equilibrating pair of pyramidal radicals shown in Figure 1. More information about radical structure is found in Chapter 6 of Volume I.) Support for a radical mechanism for a reaction such as that shown in Scheme 2 rested, at the time, primarily on this type of reaction being promoted by radical initiators and inhibited by radical scavengers.\textsuperscript{4} Primary evidence that halogenated carbohydrates react with tin hydrides to produce free radicals came later with direct observation of these radicals by ESR spectroscopy (eq 2).\textsuperscript{8}
B. Reactivity of Halogenated Compounds

Kinetic studies on reactions of alkyl halides with tri-\(\text{n}\)-butyltin hydride show that the rate determining step in these simple reduction reactions (Scheme 3) depends on the type of alkyl halide undergoing reaction.\(^9,10\) For alkyl iodides and bromides this step is the hydrogen-atom abstraction reaction shown in eq 3. Hydrogen-atom abstraction remains rate determining for reactive alkyl chlorides, but for chlorides that are not activated in some manner, abstraction of the chlorine atom by an organotin radical takes on the rate-determining role (eq 4).\(^9,10\) (Equations 3 and 4 are located in Scheme 3.)

\[
\text{Scheme 3}
\]

\[
\begin{align*}
R\cdot + \text{MH} & \rightarrow RH + M\cdot \quad (3) \\
M\cdot + RX & \rightarrow MX + R\cdot \quad (4)
\end{align*}
\]

MH = a hydrogen donor, often \(\text{Bu}_3\text{SnH}\)
RX = an alkyl halide or a halogenated carbohydrate

Since halogen-atom abstraction (eq 4) is not rate-determining for alkyl iodides or bromides, relative reactivity of these compounds cannot be established by measuring overall reaction rates; however, their relative reactivity can be determined by allowing pairs of alkyl halides to compete for a limited amount of \(\text{Bu}_3\text{SnH}\). Emerging from such study is the order of reactivity \(\text{RI} > \text{RBr} > \text{RCl} >> \text{RF}\).\(^3,4,7,10,11\) (Fluorinated compounds are effectively unreactive.\(^6,10\)) A similar reactivity order exists for reaction of halogenated compounds with \((\text{Me}_3\text{Si})_3\text{SiH}\).\(^12,13\)

Absolute rate constants for reaction of alkyl halides with tri-\(\text{n}\)-butyltin and tris(trimethylsilyl)silyl radicals can be measured by flash-photolysis techniques. For halogen-atom abstraction from alkyl iodides with \(\text{Bu}_3\text{Sn}\cdot\) and \((\text{Me}_3\text{Si})_3\text{Si}\cdot\) rate constants approach those for diffusion-controlled reactions (\(k \approx 1 \times 10^9 \text{ M}^{-1}\text{s}^{-1}\)).\(^11–15\) Constants for alkyl bromide reaction are nearly as large (\(k \approx 1 \times 10^8 - 1 \times 10^7 \text{ M}^{-1}\text{s}^{-1}\)),\(^11–15\) but for alkyl chlorides that are not specially activated these rate constants typically are considerably smaller (\(k \approx 1 \times 10^4 - 1 \times 10^2 \text{ M}^{-1}\text{s}^{-1}\)).\(^11,13,15\) Since the rate constants for hydrogen-atom abstraction from \(\text{Bu}_3\text{SnH}\) and \((\text{Me}_3\text{Si})_3\text{SiH}\) by carbon-centered radicals are approximately \(2 \times 10^6 \text{ M}^{-1}\text{s}^{-1}\) and \(1 \times 10^5 \text{ M}^{-1}\text{s}^{-1}\), respectively, absolute rate constant data provide quantitative support for the conclusion that for dehalogenation of alkyl iodides and bromides the reaction shown in eq 3 is rate determining, but for typical alkyl chlorides eq 4 describes the rate determining step.\(^10\)

Within a group of compounds containing a single type of halogen atom, those that form more stable radicals by halogen-atom abstraction (eq 4) are the ones that have larger rate constants for reaction.\(^5,6\) This fact provides the basis for the order of reactivity (tertiary > secondary > primary) that characterizes each type of alkyl halide. A reaction that illustrates this reactivity difference is found in eq 5, where the secondary chlorine atom in the substrate is more reactive than the primary one.\(^16\)
C. Possible Pathways to Radical Formation

Possible mechanisms for halogen-atom abstraction by the tri-n-butyltin radical are pictured in Schemes 4 and 5. The structure for the transition state in the reaction shown in Scheme 4 has partial carbon–halogen and tin–halogen bonds\(^\text{17,18}\) and has a slight positive charge on the tin atom.\(^\text{4,19}\) In the mechanism pictured in Scheme 5 an intermediate with fully formed tin–halogen and carbon–halogen bonds (and, consequently, a hypervalent iodine atom) is proposed. Although some homolytic substitution reactions are believed to involve hypervalent atoms,\(^\text{18,20}\) molecular orbital calculations indicate that reactions of alkyl halides do not produce such intermediates.\(^\text{17,18}\)

\[
\text{Scheme 4}
\]

\[
\text{RX} + \cdot \text{SnBu}_3 \rightarrow \begin{array}{c}
\delta^+ \\
\delta^-
\end{array} \rightarrow R \cdot + X\text{Bu}_3
\]

\[
\text{Scheme 5}
\]

\[
\text{RX} + \cdot \text{SnBu}_3 \rightarrow \begin{array}{c}
R - \cdot \\
X - \text{SnBu}_3
\end{array} \rightarrow R \cdot + X\text{SnBu}_3
\]

A third proposal for radical formation begins with electron transfer from Bu\(_3\)Sn· to a halogenated compound to produce Bu\(_3\)Sn\(^+\) and a radical anion (Scheme 6).\(^\text{21,22}\) The radical anion then dissociates to give a carbon-centered radical and a halide ion. A variation on this proposal (also pictured in Scheme 6) has electron transfer occurring simultaneously with carbon–halogen bond cleavage. Study of electron transfer to alkyl halides from Bu\(_3\)Sn· indicates that this reaction is not likely to occur unless the substrate contains an iodine atom and produces a stabilized radical.\(^\text{22}\) [This restriction to iodine-containing compounds does not apply to more reactive electron donors. Electron transfer from active metals and during electrochemical reactions takes place to glycosyl bromides (Section III.D). Organometallic complexes also transfer electrons readily to both carbohydrate iodides and bromides (Section III.B.2).]

\[
\text{Scheme 6}
\]

\[
\text{RX} + \cdot \text{SnBu}_3 \rightarrow R - \cdot \text{SnBu}_3
\]

\[
R \cdot + X\text{SnBu}_3
\]

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