

Chapter 1

Free-Radical Reactions in Carbohydrate Chemistry

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I. The Emergence of Free-Radical Reactions

The success of free-radical reactions in chemical synthesis is one of the remarkable developments in chemistry during the past several decades. Investigation and application of these reactions continues unabated at present and shows no sign of decreasing in the future. To appreciate the rapid rise of free-radical reactions to their position of prominence in the synthesis of organic compounds, it is only necessary to compare the wealth of information in existence today with the modest amount of material that was available prior to the 1970s. This comparison is easily done by consulting some of the many books and review articles describing the development of various aspects of free-radical chemistry during the past several decades.¹⁻¹⁰⁶ (Free-radical polymer formation has a different history. Considerable information on this topic existed prior to the 1970s.)

Once extensive investigation began, synthetic, free-radical chemistry matured so rapidly that by 1993 it was possible to state with confidence that “radical reactions, even with highly complex and heavily substituted substrates, can be conducted in a highly selective and efficient manner.”²³ Assessments such as this, which continue to be reinforced as additional discoveries are made, leave little doubt about the importance of radical reactions; yet, chemists saw these processes much differently earlier in the 1900s. In reflecting on these earlier times, the pioneering, free-radical chemist C. Walling noted that most chemists considered radical reactions to be “messy, unpredictable, unpromising and essentially mysterious”.⁷

What caused such a dramatic change in attitude toward radical reactions? Undoubtedly there were a number of reasons, but several are particularly noteworthy. One of these is the discovery of radical-based reactions for such synthetically important transformations as extending carbon-atom chains, creating new ring systems, and altering substitution patterns. Another decisive factor is the sophistication, based largely on careful measurement of rate constants, that researchers developed in adjusting reaction conditions to favor specific pathways. Also influential is the information discovered about ways to conduct radical reactions under mild conditions. All of these factors participated in changing attitudes toward free-radical reactions to the point that these reactions be-

came recognized as powerful synthetic tools and considered to be valuable compliments to their ionic counterparts.¹⁰⁷

II. The Role of Free-Radical Reactions in Carbohydrate Synthesis

The characteristics of free-radical reactions are well suited for transformation of multifunctional compounds such as carbohydrates. The presence of many functional groups in a compound can open a variety of easily activated reaction pathways; consequently, any mild reaction that accomplishes a desired structural change in the face of many possible changes is greatly prized. The high levels of selectivity and mild conditions characteristic of many radical reactions make these processes particularly attractive for carbohydrate synthesis.

III. Chain Reaction: A Natural Pathway for Free-Radicals

Free radicals in solution tend to combine with each other at rates that are close to the highest possible, that is, rates approaching those at which reactants diffuse through a solution.¹⁰⁸ Rapid radical combination dictates that to observe other radical reactions, a low concentration of radical intermediates must be maintained. The problem of avoiding radical combination and, at the same time, promoting other radical reactions finds a natural solution in the use of chain reactions. Efficient chain reactions are processes in which each of a small number of radicals starts a sequence of reactions that is repeated many times before a reaction such as radical combination terminates the chain. The match between the need to maintain low radical concentration and the benefit that low concentration brings to chain reactions naturally leads to many of the most useful, free-radical reactions being chain processes. It is reasonable (perhaps mandatory), therefore, to begin describing free-radical chemistry with a detailed discussion of chain reactions. Such a discussion is the focus of the next chapter.

IV. References

Most of the references cited in this chapter are to review articles. Since the majority of these articles focus on a particular aspect of free-radical chemistry, the title of each is included in parenthesis as a guide to article content. In later chapters this additional information is not really necessary; consequently, article titles will not be added to the references in other chapters.

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