the impressive richness of Nature in terms of molecular complexity and beauty, biological activity, and laboratory synthetic challenge. Behind these structures are hidden numerous golden opportunities for discovery, enrichment of the art and science of total synthesis in particular and organic synthesis in general, synergy studies with biology and medicine, and education and training of young practitioners of organic synthesis. The latter students will be equipped with knowledge, expertise, and inspiration to apply their skills for the benefit of science and society in the future.

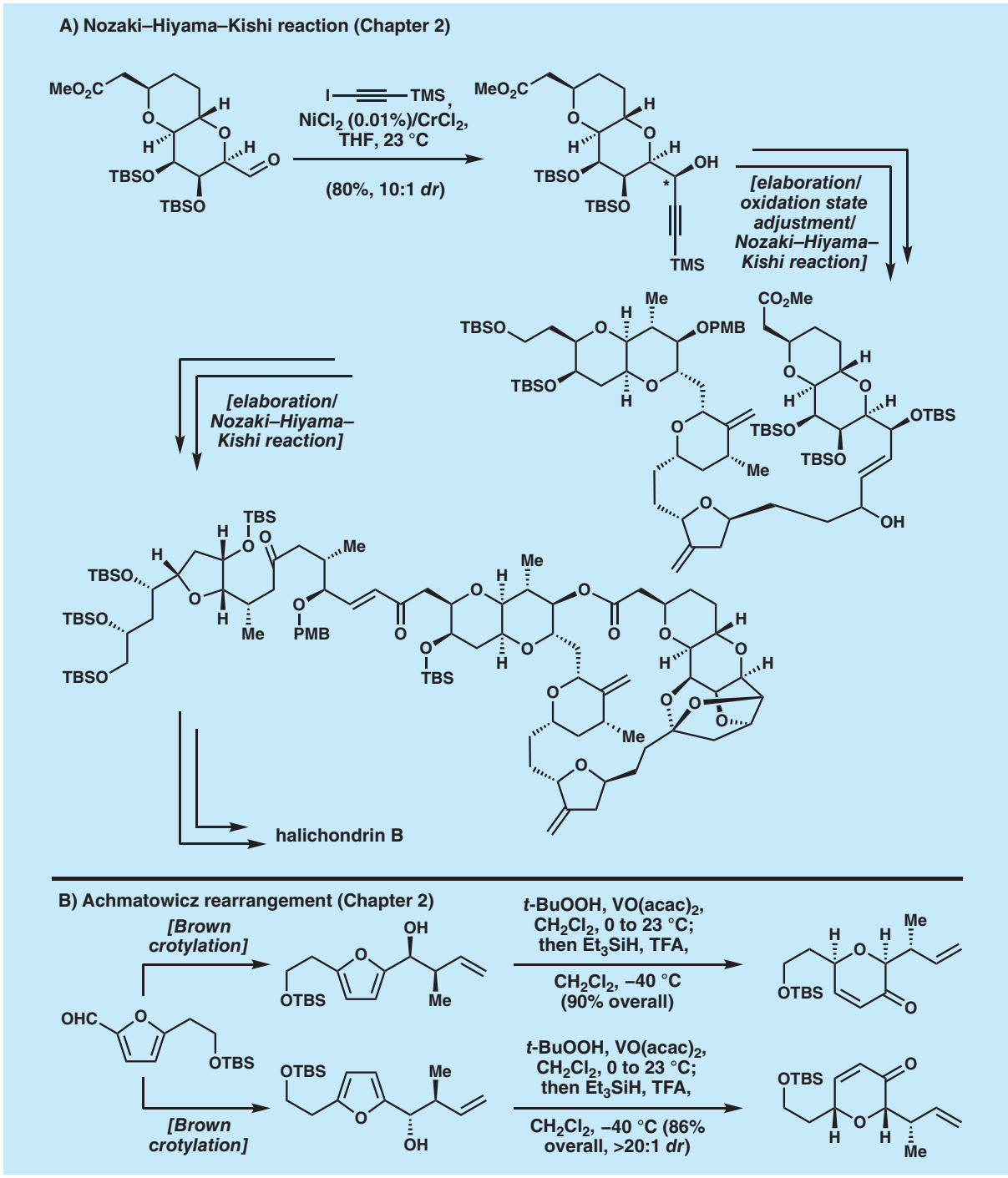
In going through the Chapters of this book, one can learn of the efforts of the pioneers to synthesize each naturally occurring molecule and, in many instances, their analogues for biological investigations. Although not all the time, in several cases, the path of the practitioner leads to drug candidates for clinical trials and beyond, thus enriching the repertoire of medicines for curing diseases, such as in the case of halichondrin B (Figure 1). In that case, the simpler analogue, eribulin, became an anticancer drug (brand name Halaven), available today from the Japanese company Eisai, for the treatment of patients suffering from breast cancer or liposarcoma. For sure, Nature holds further secrets waiting to be discovered and developed just as so many other discoveries were translated into therapies through design and chemical synthesis of natural products in the past. A number of such investigations will be mentioned in this book in addition to new synthetic methods and strategies for organic synthesis, constituting new advances in the field of total synthesis and its neighboring disciplines.

1.2 Methods and Strategies

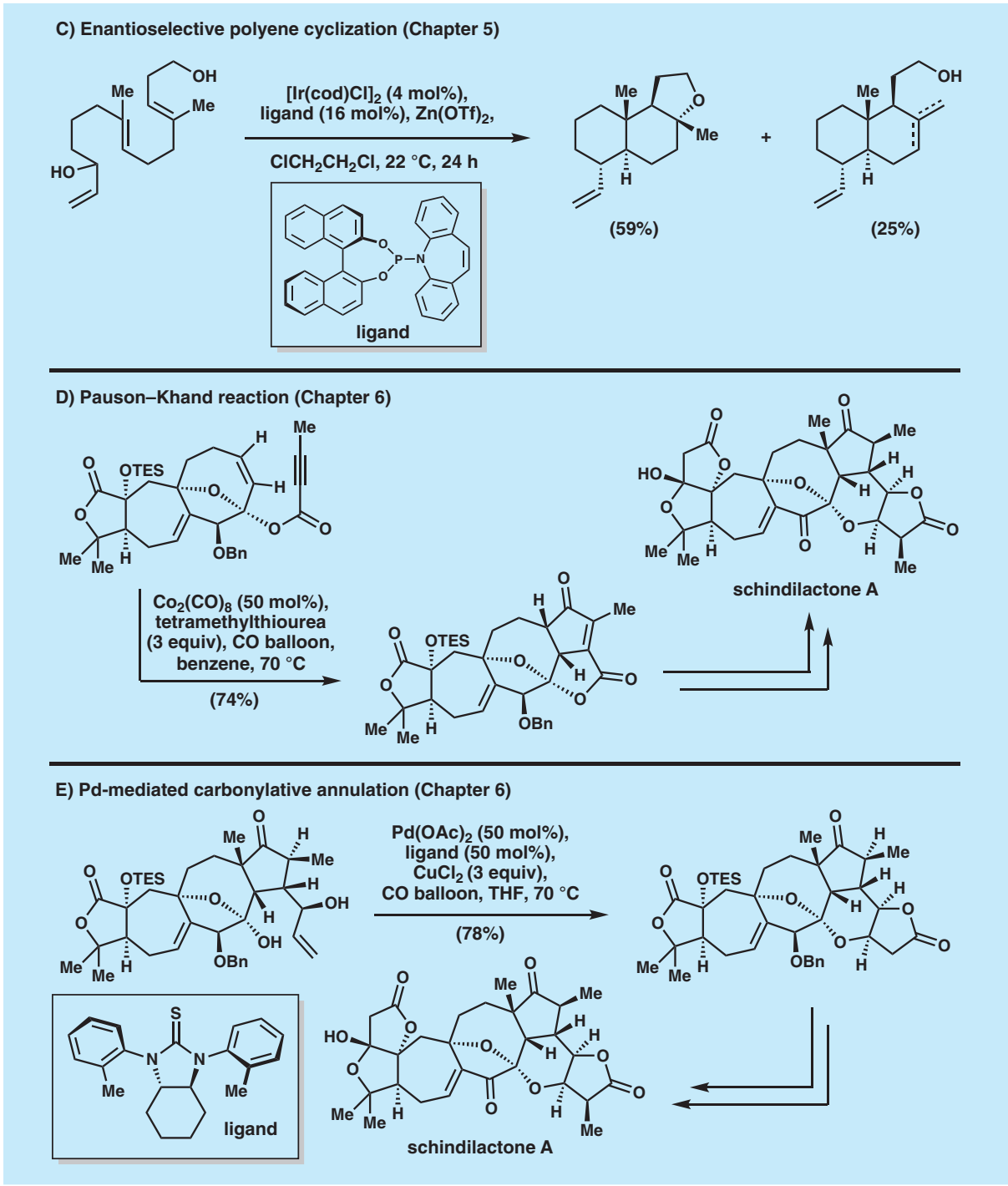
As organic synthesis advances, new methods become available for deployment and testing in total synthesis. Thus, in addition to the improvements of well-established methods and catalysts, totally new reactions and facilitators have appeared in the last few years, a number of which are included in some of the Chapters as updates in the field. Examples include C−H-activation/functionalization, photoredox catalysis, electrosynthesis, hydrogen atom transfer (HAT)-initiated radical reactions, and transformations catalyzed by engineered enzymes (integration of enzymatic reactions with traditional synthetic organic reactions within total synthesis strategies), among others. Scheme 1 highlights a number of such novel reactions and/or reagents or catalysts and their applications.

1.3 Classics in Total Synthesis IV

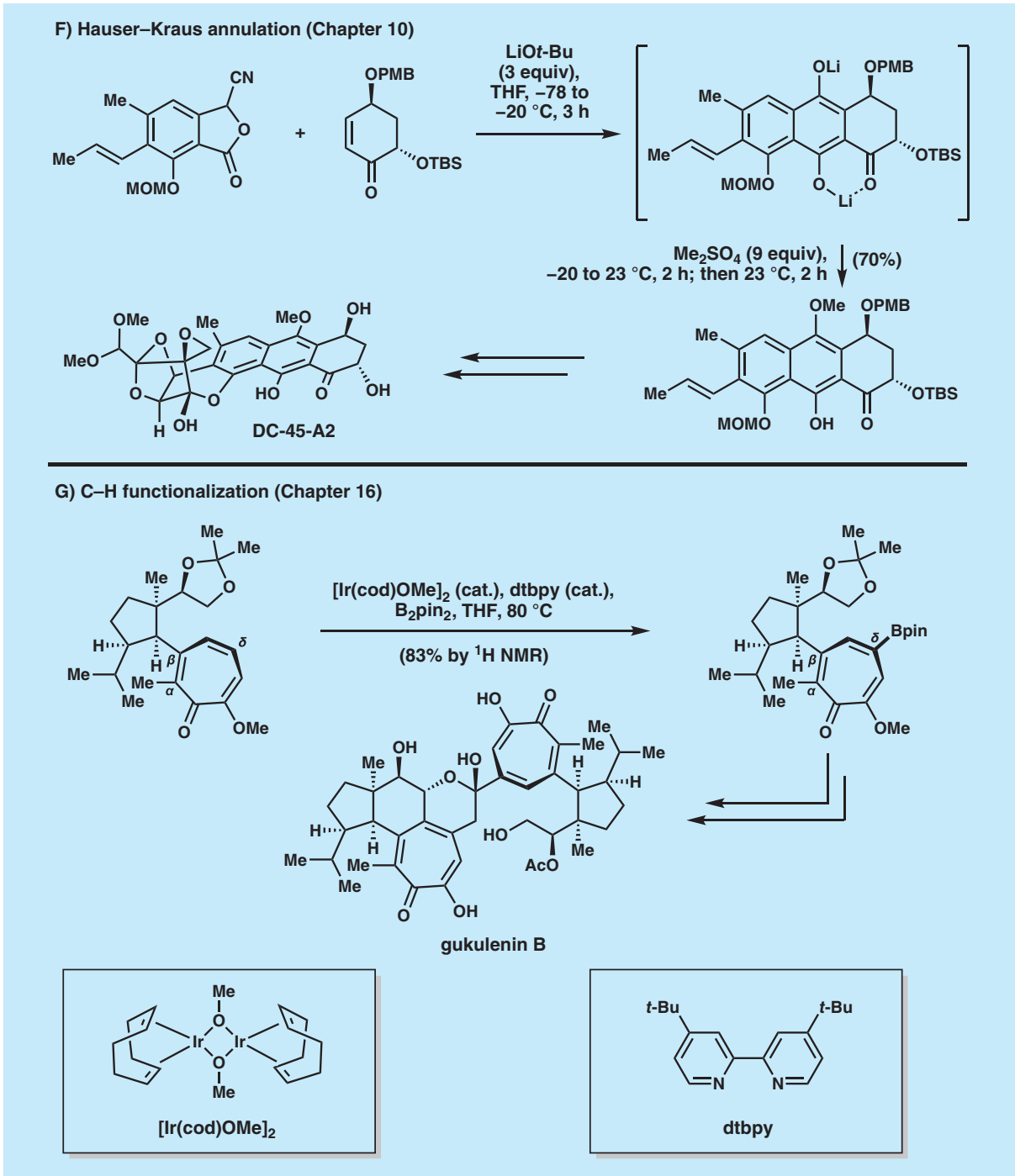
As a continuation of our series of *Classics in Total Synthesis*, we include in this edition a number of the latest endeavours in the field with appropriate references to older campaigns on the same or similar target molecules. We attempted to reflect as much diversity as



Scheme 1. Representative examples of selected methodologies featured.



Scheme 1. Representative examples of selected methodologies featured (continued).



Scheme 1. Representative examples of selected methodologies featured (continued).

possible, both with regard to the target molecules and the laboratories from where the works were published. Particular emphasis was placed on the latest trends in strategy and relevance of the work to translational aspects and applications to biology and medicine and other impacts of the work, including on the advancement of total synthesis for its own sake. We continued the inclusion of an artistic frontispiece that we introduced in *Classics in Total Synthesis III*. We hope and trust that the readers of this pedagogical book will find it enjoyable, inspirational, and rewarding. We congratulate all those faculty and students who contributed to the total synthesis achievements described in this volume, and we wish its readers all the best in their endeavours involving this special art and science of replicating the molecules of Nature, and others like them, in the laboratory. Needless to say, many more brilliant total syntheses were accomplished by other groups that, unfortunately, we could not accommodate in this volume. We apologize to the authors of those total syntheses and encourage students to study the related publications carefully to further enrich their knowledge and inspire them for continued advances in the field.