

nesium was first activated by stirring overnight over BuLi, followed by decantation of the activator before attempting to initiate the reaction (reaction 2). Addition of NaI (reaction 3) or CoCl₂ (reaction 4) was also to no avail, except after an induction period of 7 days, when reaction began, using CoCl₂ as a catalyst. The reaction is slow; however, the fluoro Grignard was produced in 95% yield after 21 days.

Addition of a catalytic amount of Br₂ (reaction 5), I₂ (reaction 6), ethylene dibromide (reaction 7), and ethyl bromide (reaction 8) also catalyzed the formation of the fluoro Grignard compound. The best results were obtained when I₂ (4%) produced a 95% yield of the fluoro Grignard compound in only 6 days. It is interesting to note that the yield remained constant after an additional 8-day reflux period, whereas when ethylene dibromide and magnesium powder were used, the yield decreased from 88 to 42% during an additional 15-day reflux period. A catalytic amount of ethyl bromide (reaction 8b) produced a high yield (94%) of the fluoro Grignard compound in 22 days. The reaction time can be substantially shortened by addition of larger amounts of ethyl bromide (reactions 8c and d). The latter reactions are essentially entrainment reactions, which have been reported earlier for use in the preparation of chloro, bromo, and iodo Grignard compounds that are difficult to form.¹⁰

Attempts to prepare alkylmagnesium fluorides by indirect methods have also been attempted. No redistribution occurred when diethylmagnesium was allowed to react with magnesium fluoride (Alfa Inorganics Co.) in Et₂O-THF for 3 days (reaction 9).¹¹ No metal-

(10) V. Grignard, *C. R. Acad. Sci., Paris*, **198**, 625 (1935); see M. S. Kharasch and O. Reinmuth, Ed., "Grignard Reactions of Nonmetallic Substances," Prentice-Hall Inc., New York, N. Y., 1954, pp 38-45.

halogen exchange took place between diethylmagnesium and hexyl fluoride in Et₂O-THF during 6 days (reaction 10a). However the exchange occurred very slowly in the presence of a catalytic amount of cobalt chloride (reaction 10b).

Both ethyl- and hexylmagnesium fluoride were allowed to react with H₂O, O₂, CO₂, C₆H₅CN, and (C₆H₅)₂C=O and the results compared with the results of the same reactions using ethyl- and hexylmagnesium bromide. In all cases the fluoro and bromo Grignard compounds produced the expected product in comparable yields. The fluoro Grignard compounds did react faster than the corresponding bromo compounds toward benzophenone, and gave a higher ratio of addition to reduction.

Studies now in progress involve the extension of the reaction to other alkyl and aryl fluorides and other solvents. Molecular association and nmr studies will be carried out in an attempt to establish the composition of the fluoro Grignard compounds in solution. Work is also in progress to determine the stereoselective nature of the fluoro Grignard compounds as alkylating agents.

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(11) This reaction was previously reported informally by Dessy;¹² however no official report has appeared up to this time. We do not maintain here that magnesium fluoride from some other source will also be inert to redistribution. This possibility is presently being explored.

(12) R. E. Dessy, *Chem. Eng. News*, **38**, (31), 42 (1960).

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Book Reviews

Catalysis in Chemistry and Enzymology. By WILLIAM P. JENCKS, Graduate Department of Biochemistry, Brandeis University, Waltham, Mass. McGraw-Hill Book Co., New York, N. Y. 1969. xvi + 644 pp. 15 × 23 cm.

In the opening chapter of the book Jencks quotes Berzelius who said, "This easy kind of physiological chemistry is created at the writing desk and is the more dangerous, the more genius goes into its execution." After reading Jencks' book a paraphrase of this quotation might be "This sophisticated kind of physical organic chemistry was created at the writing desk and appears more simple, the more genius goes into its elucidation." This 644-page book is a penetrating, scholarly yet readable analysis of the mechanisms underlying enzymatic reactions.

The book as a whole is devoted to the explanation and analysis of those physical organic mechanisms which pertain directly to enzyme catalysis and their application in illustrative enzymatic examples. As a result, solution chemistry is emphasized to the virtual exclusion of gas-phase kinetics, quantum mechanical calculations, and other areas which might be chapters in a more chemically oriented book. Having chosen the subjects which he considers relevant to the enzyme mechanism, Jencks discusses them from the point of view of the physical organic chemist. Yet in the areas

chosen he proceeds to the frontiers of present knowledge and maintains the rigor of good physical organic chemistry.

In the first chapter entitled "Approximation," Jencks considers the catalytic consequences of juxtaposition of substrates and catalysts at the surface of an enzyme. This is treated both theoretically and empirically with examples of intramolecular reactions and their relative accelerations compared to intermolecular reactions. Nonenzymatic models in which two molecules are associated by complex formation simulating enzyme-substrate complexes and heterogeneous catalysis are also discussed.

In the second chapter, "Covalent Catalysis" is analyzed. The chapter opens with criteria for the delineation of enzyme-substrate intermediates and the kinetic consequences of such intermediates. It then proceeds to the correlation of structure with nucleophilicity of the attacking atom. Emphasis is on reactions of carbonyl compounds and pyridoxal reactions. The effect of structure on the reactivity of the leaving group is discussed extensively, and the chapter concludes with a brief analysis of oxidative catalysis.

The third chapter deals with general acid and base catalysis. In this chapter the opening pages are largely devoted to model systems. Application to enzymes is exemplified through chymotrypsin and aconitase. The chapter then proceeds to more complex examples and the problems of defining the transition state.

Chapter 4 deals with isotope effects and is a masterful chapter which threads its way through a difficult subject briefly and perceptively. This chapter avoids the usual overstatements and claims for isotope effects without losing the important information which can be gained from such experiments. Chapter 5 on strain distortion and conformation change deals with a subject which is close to Jencks' heart, but the author deals with this subject objectively and faces some of the difficult consequences unflinchingly. He ends the chapter with good examples from enzymatic and non-enzymatic sources.

The second part of the book deals with the fundamental forces in aqueous solution relevant to enzyme structure and action. Chapters on the hydrogen bond (Chapter 6), electrostatic interactions (Chapter 7), hydrophobic forces (Chapter 8), and donor-acceptor and charge transfer complexes (Chapter 9) each analyze these forces so necessary for understanding protein structure and the interactions of ligands with the protein surface.

Chapter 10 in part III is an application of many of the principles and techniques developed in previous chapters for a particular class of reactions. In this chapter on carbonyl and acyl-group reactions, the analysis of nonenzymatic reactions is merged with an analysis of specific enzymes, most particularly chymotrypsin. It illustrates how far one may proceed in a detailed analysis of enzyme mechanisms in terms of known physical organic chemistry. A final chapter entitled "Practical Kinetics" is a short course in kinetics for the student who has had only a brief exposure to this subject. It strips kinetics of its mathematical calisthenics and its uncritical claims and discusses it in terms of practical application to real problems. As such it is invaluable for a student, and it was surprising and instructive to this reviewer to see how ably and briefly Jencks has evaluated the information which can be obtained and the pitfalls which must be avoided.

The introduction states that the book is based on material presented in a one-semester course assuming a background in physical chemistry and advanced organic chemistry. This reviewer's opinion is that this text is practically ideal for such a course with students of this level of sophistication. The book contains a skillful melding of theoretical analyses and specific examples. The reader will have to take time to analyze the examples if he is to absorb the full significance of the text, but if he is willing to spend this time the rewards will be very great. An organic chemist wishing to be exposed to enzyme mechanisms or an enzyme chemist wishing to learn some physical chemistry can take a less dedicated approach by skipping some of the detailed examples. He may emerge less sophisticated in the details of physical organic chemistry but he will be aware of the fundamentals.

The book is not comprehensive. Its emphasis in mechanisms tends to follow the author's interests. Oxidative mechanisms, for example, are almost ignored. Some enzyme types are mentioned casually or not at all. To cover these in addition would have required many more pages or a more superficial treatment of the examples presented. The author has selected a solid center of enzyme mechanism and provided the basis for understanding less established examples.

A good book is a work of art and this is a very good book. It makes things simple but does not oversimplify. It provides documentation but does not drown the reader in facts. It is appropriately illustrative rather than superficially comprehensive. Many students will learn the fundamentals of enzyme mechanisms from this book and they cannot ask for a better source.

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