Neighboring Group Participation

Volume 1

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WITHDRAWN

Brian Capon
The University
Glasgow, Scotland

and

Samuel P. McManus
The University of Alabama in Huntsville
Huntsville, Alabama

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Preface

Neighboring group participation is a term which encompasses all intramolecular reactions and all reactions which involve nonelectrostatic through-space interactions between groups within the same molecule. The term was invented in 1942 by Saul Winstein, whose many contributions to the growth and maturing of the subject are unequaled. Although the inventor of the term, Winstein was not the first worker to study neighboring group participation. An examination of Beilstein will show that many intramolecular reactions were known to the synthetic organic chemist well before the turn of the century, and as early as 1891 W. P. Evans, working at Giessen, described a kinetic investigation of the base-promoted cyclization of ethylene chlorohydrins to ethylene oxides—an important intramolecular reaction. He was followed some twenty years later by Freundlich, whose valuable studies on participation by the amino group began to appear in 1911. Freundlich was later joined by Salomon, who by the mid-thirties had developed a reasonable understanding of the efficiency of the neighboring amino group in acyclic systems. In the late twenties to mid-thirties the subject began to expand with the work of Bennett on participation by thioether groups, Nilsson and Smith on neighboring hydroxyl, and Caldin and Wolfenden on neighboring carboxylate, and with discussions of the dependence of cyclization rates on ring size by Ruzicka, Salomon, and Bennett. This background, along with the elegant studies of Hughes and Ingold on aliphatic nucleophilic substitution, set the stage for the entrance of Winstein. Also about this time Isbell proposed a process similar to that proposed by Winstein for the neighboring acetoxy group, viz., "the intramolecular orthoester reaction," but it was the influence of Winstein that caused the subject to become recognized as all-pervasive in organic chemistry.

Examples of neighboring group participation constantly occur with

all classes of organic compounds, including organometallic compounds and natural products. The analogy between neighboring group participation and the intracomplex interactions of the functional groups of an enzyme and those of the substrate is well known. In addition, some steps in enzyme reactions are true examples of neighboring group participation, such as the deacylation of an acyl enzyme or the deprotonation of the Schiff base formed by a class I aldolase and its substrate.

It is obviously impossible to write a comprehensive monograph on a subject as broad as this, since too many examples are hidden away in papers whose titles (and, in many cases, abstracts) give no mention of a relationship to neighboring group participation. We have not, therefore, set out to write a book which is comprehensive, but one which treats the subject in a systematic and critical way, while trying not to omit any significant examples. We realize of course that some readers will not agree with our interpretation of what is significant and we welcome comments on this score. Perhaps because of a different perspective our interpretation of the experimental results differs in some instances from that of the original investigators; we hope that from the way in which the discussion is presented the reader will be able to tell this.

To make this undertaking manageable we have chosen to divide the material into two volumes. The first part of the present volume is a general introduction and it includes a discussion of some factors which may account for the fast rates observed for reactions occurring with neighboring group participation and some ways in which neighboring group participation is experimentally evaluated. The second part of this volume contains a systematic treatment of simple oxygen, sulfur, and nitrogen groups. The second volume will include a treatment of other simple groups, e.g., the halogens, carbon, hydrogen, etc., and of complex groups, e.g., amides, esters, organometallic compounds, etc. In addition, a survey of neighboring group participation in key reactions, e.g., reduction, hydrolysis, etc., will be included. In the present volume we have tried to cover the literature through the middle of 1975, although a few papers appearing later than this were inserted during the production process.

We are indebted to the individuals whom we acknowledge in the text for supplying unpublished results or for discussion of results. One of us (S.P.M.) would particularly like to acknowledge the Chemistry faculty of the University of South Carolina for the warm hospitality afforded him during his tenure as a visiting faculty member during 1974–75. It was during this time that much of his material for this volume and some for the

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BRIAN CAPON
SAMUEL P. MCMANUS

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