

Topics in
STEREOCHEMISTRY

E.L. Eliel S.H. Wilen & N.L. Allinger
EDITORS

Volume 15

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STEREOCHEMISTRY

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VOLUME 15

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**TOPICS IN
STEREOCHEMISTRY**

VOLUME 15

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To the memory of
SAN-ICHIRO MIZUSHIMA

INTRODUCTION TO THE SERIES

It is patently impossible for any individual to read enough of the journal literature so as to be aware of all significant developments that may impinge on his or her work, particularly in an area such as stereochemistry, which knows no topical boundaries. Stereochemical investigations may have relevance to an understanding of a wide range of phenomena and findings irrespective of their provenance. Because stereochemistry is important in many areas of chemistry, comprehensive reviews of high quality play a special role in educating and alerting the chemical community to new stereochemical developments.

The above considerations were reason enough for initiating a series such as this. In addition to updating information found in such standard monographs as *Stereochemistry of Carbon Compounds* (Eliel, McGraw-Hill, 1962) and *Conformational Analysis* (Eliel, Allinger, Angyal, and Morrison, Interscience, 1965; reprinted by American Chemical Society, 1981) as well as others published more recently, the series is intended also to deal in greater detail with some of the topics summarized in such texts. It is for this reason that we have selected the title *Topics in Stereochemistry* for this series.

The series is intended for the advanced student, the teacher, and the active researcher. A background of the basic knowledge in the field of stereochemistry is assumed. Each chapter is written by an expert in the field and, hopefully, covers its subject in depth. We have tried to choose topics of fundamental importance aimed primarily at an audience of inorganic and organic chemists but involved frequently with basic principles of physical chemistry and molecular physics, and dealing also with certain stereochemical aspects of biochemistry.

It is our intention to produce future volumes at intervals of one to two years. The editors will welcome suggestions as to suitable topics.

We are fortunate in having been able to secure the help of an international board of editorial advisors who have been of great assistance by suggesting topics and authors for several chapters and by helping us avoid, in so far as possible, duplication of topics appearing in other, related monograph series. We are grateful to the editorial advisors for this assistance, but the editors and authors alone must assume the responsibility for any shortcomings of *Topics in Stereochemistry*.

E. L. ELIEL
S. H. WILEN
N. L. ALLINGER

PREFACE

Volume 15, as did many of the previous volumes, contains four chapters. The first one, by Frank-Gerrit Klärner, deals with "walk rearrangements" (also called "circumambulatory rearrangements") in [n.1.0] bicyclic compounds, both neutral and ionic. These are rearrangements in which a divalent group, for example CR_2 , NR , O , S , which forms part of a three-membered ring, undergoes a migration along the surface of a cyclic π -system. The scope of these rearrangements, which themselves are manifestations of the Woodward-Hoffmann rules, is greatly enlarged because numerous cyclopentadienoid and heterocyclopentadienoid systems may be photochemically converted, by electrocyclization, to [2.1.0] bicyclopentene systems, which may then undergo walk rearrangements and subsequently be thermally reopened to rearranged cyclopentadienoids. Alternate mechanisms are possible, and a number of these rearrangements are discussed in detail.

The second chapter, by Robert J. P. Corriu, Christian Guérin, and Joël J. E. Moreau, constitutes a monumental review of stereochemistry at silicon. This subject was last discussed comprehensively in a pioneering book by L. H. Sommer in 1965, with a brief 1973 update. In the present chapter the authors bring the literature up to date, discussing silicon stereochemistry in all of its aspects, especially with a view to reaction mechanism, in which area they have made a number of original contributions. This chapter will no doubt become required (and welcome) reading for anyone involved in any way with silicon stereochemistry.

The third chapter, by Masao Nakazaki, is concerned with the synthesis and stereochemistry of chiral organic molecules with high symmetry. It was recognized many years ago that the presence of symmetry axes in a molecule is no bar to chirality and the term dissymmetry has, in fact, been coined to imply that chiral molecules need not be asymmetric. In 1974, in the van't Hoff-Le Bel Commemorative Issue of *Tetrahedron*, M. Farina and C. Morandi collected what was then a fairly comprehensive list of chiral molecules of C_n ($n > 2$), D_n , and higher symmetry. Nakazaki who, himself, has synthesized a sizeable number of molecules of this type, now brings the subject up to date with an extensive list of new and often quite intriguing molecules of C_3 , D_2 , D_3 and higher symmetry. Much ingenuity has gone into the synthesis of such molecules.

The fourth and final chapter, by Heinz G. Floss, Ming-Daw Tsai, and Ronald W. Woodard leads into the realm of biochemistry, dealing with the stereochemistry of biological reactions at propochiral centers. Prochiral centers are centers

of the type AX_2YZ , where A is generally a tetrahedral central atom such as carbon or tetracoordinate phosphorus; their stereochemistry is generally probed by replacing the prochiral center by a chiral one $AXX'YZ$, where X and X' are different isotopes of the same atomic number. For example, in Westheimer and Vennesland's classical work, the prochiral methylene center in CH_3CH_2OH has been investigated stereochemically by replacing it with a chiral center as in CH_3CHDOH . Propochiral centers AX_3Z bear the same relation to prochiral centers $AX_2X'Z$ as prochiral centers bear to chiral ones. Probing their stereochemistry is quite an intricate task and requires double isotopic substitution of the type $AXX'X''Z$ to create a true chiral center. Examples are $CHDTCO_2H$, first synthesized chirally and analyzed by Arigoni and by Cornforth, and $[ROP^{16}O^{17}O^{18}O]^{2-}$, synthesized and stereochemically diagnosed by Jeremy Knowles, John Gerlt, and Gordon Lowe. The present chapter deals with the detection of these propochiral groups (or their isotopically labeled chiral analogs) and with their use in the probing of the stereochemistry of enzymatic reactions.

We must report, with sadness, the death of San-ichiro Mizushima on August 3, 1983. Professor Mizushima had been one of our editorial advisors since the inception of *Topics in Stereochemistry* in 1967. As professor at the University of Tokyo he undertook, in the 1930s, pioneering research concerned with the conformation of 1,2-dihaloethanes, using both dipole moment measurement and the then-novel technique of Raman spectroscopy as experimental tools. His studies culminated in the realization that these compounds, while crystallizing in the more stable anti conformation, were, in the liquid state, mixtures of gauche and anti-conformational isomers. This work is among the earliest leading to an understanding of the conformational behavior of acyclic molecules.

Mizushima had a deep understanding of the West as well as the East and, throughout his life, acted as a bridge between the two cultures. We shall miss his friendship and his advice.

ERNEST L. ELIEL
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Chapel Hill, North Carolina
New York, New York
Athens, Georgia
September 1983

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Walk Rearrangements in $[n.1.0]$ Bicyclic Compounds

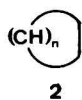
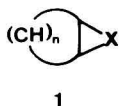
FRANK-GERRIT KLÄRNER

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I. INTRODUCTION

$[n.1.0]$ Bicycles of type 1 are homologous to annulenes of type 2. The question of homoaromaticity of these systems has been the subject of repeated theoretical and experimental investigations (1). The homoaromatic or homoantiaromatic character depends on the extent of interaction between the orbitals of the three-membered ring and the π -orbitals of the unsaturated bridge.



The walk rearrangement in an $[n.1.0]$ bicycle has been defined as a reaction in which the divalent group X (e.g., CR_2 , NR, O, S) that is part of a three-membered ring undergoes a migration along the surface of a cyclic π -system (2).

The term "walk rearrangement" used in this review is one of many that have been introduced into the literature to describe this type of reaction. Other illustrative descriptions include terms like "bones rearrangement," "merry-go-round," "ring runner," "circumambulation," and the more general "degenerate rearrangement."

Under the topic "circumambulatory rearrangements" R. F. Childs (3) has recently reviewed migrations of mono-, di-, tri- and tetravalent groups around the periphery of a ring. Walk rearrangements of [*n*.1.0] bicycles are included as one topic of this more general review.

The study of walk rearrangements has been important for developing and testing theoretical concepts in organic chemistry. Within the scope of the theory of sigmatropic reactions, Woodward and Hoffmann (4) have pointed out detailed stereochemical and topological consequences of orbital-symmetry controlled processes. In this chapter, mechanistic and theoretical aspects are examined in connection with individual examples of walking systems. In order to be able to compare the properties of closely related systems, the [*n*.1.0] bicycles are divided in two classes of compounds: neutral compounds with *n* even (*n* = 2, 4, 6, . . .), and ionic compounds with *n* odd (*n* = 1, 3, 5, . . .). Radical systems that do not fit into either of these two classes are discussed in the context of corresponding [*n*.1.0] bicycles having the same skeleton.

II. WALK REARRANGEMENTS IN NEUTRAL [*n*.1.0] BICYCLIC COMPOUNDS

A. Bicyclo[2.1.0]pent-2-ene

In a large number of five-membered heterocycles, a photochemical isomerization is observed leading to a redistribution of the ring atoms (5). In the explanation of this unusual reaction, two general types of mechanism may be discerned.

1. Electrocyclization followed by a walk of ring atom 5 in the intermediate heterobicyclo[2.1.0]pent-2-ene [path (a) in Figure 1].

2. A sequence of 1,3 shifts involving heterovinylcyclopropenes as intermediates [path (b) in Fig. 1].

Additional scrambling of the ring atoms can be achieved by further rearrangement, following path (a) as well as path (b).

Table 1 contains several examples of phototranspositions of five-membered heterocycles. Here the distinction between paths (a) and (b) is largely based on a comparison of the substitution pattern of starting material and product. In some cases intermediate heterovinylcyclopropenes and heterobicyclopentenenes, respectively, were actually trapped or isolated. For example, in the interconversion of

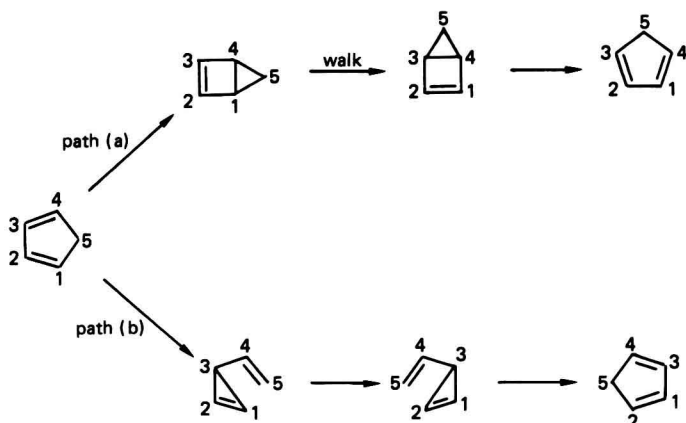


Figure 1. Possible pathways in the phototransposition of five-membered rings.

Table 1
Phototranspositions in Five-Membered Heterocycles

Entry	Reactants	Products	Reaction Path	Ref.
1	 $R^4 = \text{H, H, CH}_3$ $R^5 = \text{H, CH}_3, \text{H}$		(a)	(6)
2	 $R^1 = \text{CH}_3, \text{CH}_3, \text{t-C}_4\text{H}_9$ $R^4 = \text{H, CH}_3, \text{t-C}_4\text{H}_9$		(b)	(7)
3	 $R = \text{CH}_3, \text{CH}_2\text{C}_6\text{H}_5, \text{t-C}_4\text{H}_9, \text{C}_6\text{H}_5, \text{CN}$		(a), (b)	(7c) (7d) (8)

Table 1 (Continued)

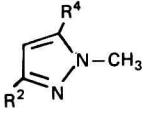
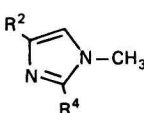
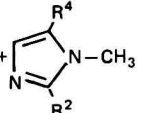
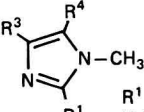
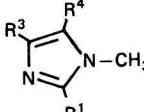
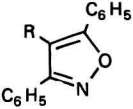
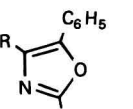
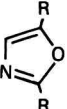
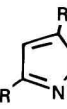
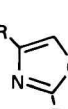
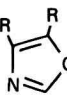





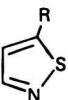
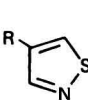
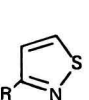
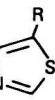

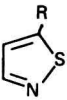

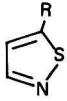


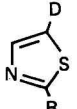


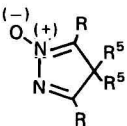
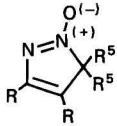
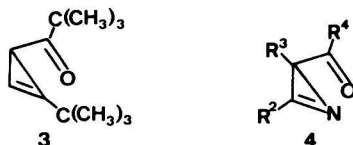
Entry	Reactants	Products	Reaction Path	Ref.
4	 $R^2 = \text{CH}_3, \text{CN}$ $R^4 = \text{CH}_3, \text{H}, \text{D}, \text{CH}_3$	 + 	(a), (b)	(9)
5	 $R^1 \quad R^3 \quad R^4$ $\text{H} \quad \text{CH}_3 \quad \text{H}$ $\text{H} \quad \text{CH}_3 \quad \text{CH}_3$ $\text{D} \quad \text{CH}_3 \quad \text{H}$		(a)	(9)
6	 $R = \text{H}, \text{C}_6\text{H}_5$		(b)	(10)
7	 $R = \text{C}_6\text{H}_5$	 +  + 	(a), (b)	(11)
8	 $R = \text{C}_6\text{H}_5$	 + 	(a), (b)	(12)
9	 $R^2 = \text{H}, \text{CH}_3, \text{H}$ $R^3 = \text{H}, \text{H}, \text{CH}_3$		(b)	(13)
10	 $R = \text{CH}_3$	 +  + 	(a), (b)	(13)
11	 $R = \text{C}_6\text{H}_5$	 + 	(a)	(14)

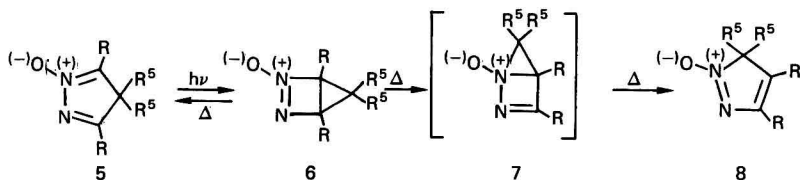
Table 1 (Continued)

Entry	Reactants	Products	Reaction Path	Ref.
12	 R = C ₆ H ₅	 + 	(a)	(14)
13	 R = C ₆ H ₅	 + 	(a)	(14)
14	 R = C ₆ H ₅ , CH ₃ R ⁵ = CH ₃ , C ₂ H ₅		(a)	(15)

2,5- into 2,4-di-*t*-butylfuran (Table 1, entry 2) or in the isoxazole → oxazole isomerization (Table 1, entry 6), the corresponding cyclopropenylketone **3** (7d) and azirinyllketone **4** (10), respectively, were characterized as intermediates.



On irradiation of 4,4-diethyl-3,5-dimethyl-4H-pyrazole-1-oxide (**5**) at -78°C (15), the valence-tautomeric heterobicyclopentene **6** was detected as the primary photoproduct. At temperatures above -20°C , **6** undergoes thermal isomerization to **5** and **8**. Product **8** is obviously formed by walk rearrangement $\mathbf{6} \rightarrow \mathbf{7}$ followed by a fast electrocyclic ring opening $\mathbf{7} \rightarrow \mathbf{8}$.



Trapping experiments and low-temperature photolysis studies indicate that a thermally induced walk rearrangement of the as yet undetected intermediate **9** is responsible for the phototransposition of several substituted pyrroles (Table 1, entry 1) (6b).