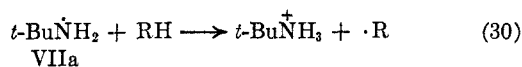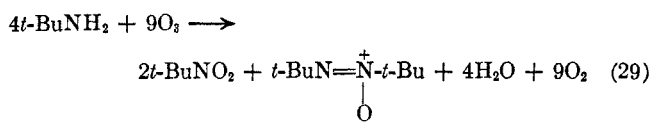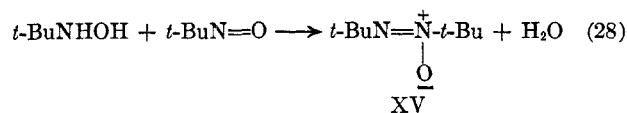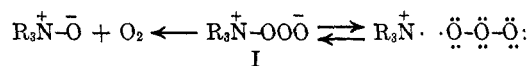alcohol products. It is noteworthy that, although the amine plays a prominent role in this oxidation of the alkane, it is not used up in the series of reactions.

$$t\text{-BuNHOH} + t\text{-BuN}{=}O \longrightarrow t\text{-BuN}{=}\overset{+}{\text{N}}\text{-}t\text{-Bu} + H_2O \quad (28)$$
$$\underset{\text{XV}}{\overset{\mid}{\underset{}{\text{O}}}}$$

$$4t\text{-BuNH}_2 + 9O_3 \longrightarrow$$

$$2t\text{-BuNO}_2 + t\text{-BuN}{=}\overset{+}{\text{N}}\text{-}t\text{-Bu} + 4H_2O + 9O_2 \quad (29)$$
$$\overset{\mid}{\underset{}{\text{O}}}$$

$$t\text{-Bu}\dot{\text{N}}\text{H}_2 + \text{RH} \longrightarrow t\text{-Bu}\overset{+}{\text{N}}\text{H}_3 + \cdot\text{R} \quad (30)$$
$$\text{VIIa}$$

$$\text{R}\cdot + \cdot O_3^- \longrightarrow \text{ROOO}^- \longrightarrow \text{RO}^- + O_2 \quad (31)$$

$$\text{RO}^- + t\text{-Bu}\overset{+}{\text{N}}\text{H}_3 \longrightarrow \text{ROH} + t\text{-BuNH}_2 \quad (32)$$
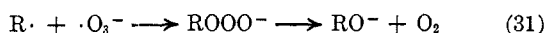
Thus, the results of ozonation of *t*-butylamine in the various solvents furnish strong evidence for two different fates of an initial amine–ozone adduct, as summarized by general eq 33. The results in carbon tetrachloride, in which an ammonium salt is produced even though the solvent does not contain hydrogen, and in isooctane, in which the solvent is converted into an alcohol even though it does not react with ozone alone, constitute especially strong evidence for nitrogen cation radical intermediates. The dissociation of I to cation and anion radicals, however, appears to become important only if the nitrogen cation radical is stabilized by resonance, as with Wurster's salts,[3] or can readily abstract a hydrogen atom from its environment.

$$\text{R}_3\overset{+}{\text{N}}\text{-}\bar{\text{O}} + O_2 \longleftarrow \text{R}_3\overset{+}{\text{N}}\text{-OO}\bar{\text{O}} \rightleftarrows \text{R}_3\overset{+}{\text{N}}\cdot \cdot\ddot{\text{O}}\text{-}\ddot{\text{O}}\text{-}\ddot{\text{O}}:$$
$$\text{I}$$

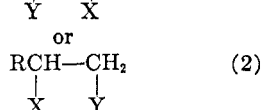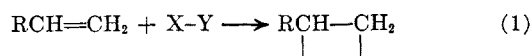# Regiospecificity. A Useful Terminology in Addition and Elimination Reactions[1]

ALFRED HASSNER

Department of Chemistry, University of Colorado, Boulder, Colorado 80302

The prefix *regio* is proposed to complement that of *stereo* to describe orientational or directional preference in reaction specificity and selectivity involving bond making or breaking. Examples of regiospecific and regioselective additions, eliminations, ring opening, and cycloadditions are discussed.

The terms stereospecificity and stereoselectivity[2] are deeply entrenched in the chemical vocabulary, particularly in that of the organic chemist. While these terms are useful in describing stereochemical preference in organic reactions, namely, the propensity to a certain relative spatial arrangement of reacting groups (*e.g. cis* or *trans* additions), there seems to be no general term in use for describing selectivity or specificity of orientational or directional preference in chemical reactions.

For instance the addition of an unsymmetrical reagent X–Y to an unsymmetrical olefin RCH=CH$_2$ often occurs in a highly specific manner, with one segment of the reagent (*i.e.*, X) being directed to assume one of two possible positions in the final product (eq 1 and 2).

$$\text{RCH}{=}\text{CH}_2 + \text{X-Y} \longrightarrow \underset{\overset{\mid}{\text{Y}}}{\text{RCH}}{-}\underset{\overset{\mid}{\text{X}}}{\text{CH}_2} \quad (1)$$
$$\text{or}$$
$$\underset{\overset{\mid}{\text{X}}}{\text{RCH}}{-}\underset{\overset{\mid}{\text{Y}}}{\text{CH}_2} \quad (2)$$

The problem is a general one, namely, that of describing the preferential making or breaking of bonds in one of two possible orientations.

We have proposed that the course of such reactions be referred to as *regiospecific*,[3] the term being derived from the latin ward *regio* denoting direction. Regiospecificity then refers to the directional preference of bond formation. If a reaction proceeds without skeletal rearrangement to give exclusively (within experimental error) one of two or more possible isomers, it is called *regiospecific*. If there is a significant preponderance of one isomer formed it is said to be *regioselective*.[4] A nearly equimolar isomer distribution is the result of a *nonregiospecific* reaction.

These terms are useful not only in addition reactions but equally in a variety of chemical processes including eliminations, ring opening, and cycloaddition reactions as illustrated below.

Although regiospecificity, like stereospecificity, describes an important characteristic of reactions by itself, selected modifying terms can greatly enhance the definition of such reactions. The terms Markovnikov[5] and anti-Markovnikov to modify the type of regiospecificity are archaic and sometimes inadequate. For instance the ionic addition of hydrobromic acid to

(1) Stereochemistry. XXXIV. For paper XXXIII, see F. W. Fowler and A. Hassner, *J. Amer. Chem. Soc.*, **90**, 2875 (1968).

(2) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., New York, N. Y., 1962.

(3) (a) A. Hassner, and F. Boerwinkle, *J. Amer. Chem. Soc.*, **90**, 216 (1968). (b) The pronunciation *reejio* is proposed. (c) The need for such a term has recently also been recognized by H. G. Viehe [*Angew. Chem. Intern. Ed. Eng.*, **6**, 767 (1967)] who proposed the slightly more cumbersome term directiospecific.
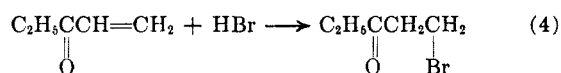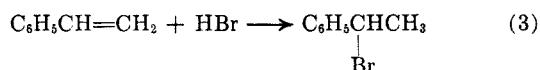
(4) Unlike in stereospecificity where one is faced with the problem of two isomeric substrates leading to the same product, in regiospecificity one deals with only one substrate leading to two (or more) possible regioisomers. This permits the designation regioselectivity to be used for partial regiospecificity.

(5) V. W. Markovnikov, *Compt. Rend.*, **81**, 668 (1875).

styrene follows Markovnikov's rule (eq 3). It is not clear whether HBr addition to ethyl vinyl ketone (eq 4)[6] should be said to be anti-Markovnikov or
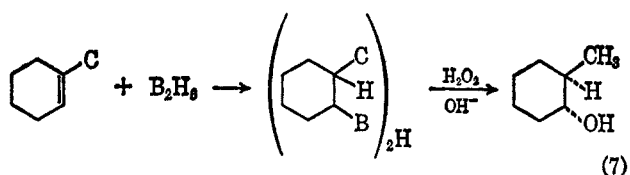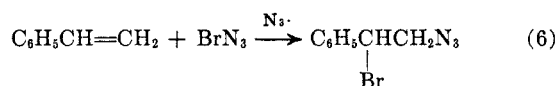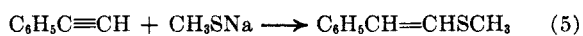
$$C_6H_5CH{=}CH_2 + HBr \longrightarrow C_6H_5CHCH_3 \quad (3)$$
$$\underset{\displaystyle Br}{|}$$

$$C_2H_5CCH{=}CH_2 + HBr \longrightarrow C_2H_5CCH_2CH_2 \quad (4)$$

whether the rule should be modified to take account of the stability of intermediate carbonium ions rather than the attachment of H$^+$ to the less substituted carbon. If specificity exists in additions to olefins of type 1 (as in eq 9), then Markovnikov's rule breaks down completely.
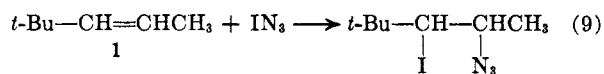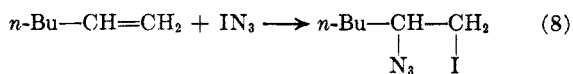
We feel it desirable that an empirical classification of orientations be employed and that the terms be chosen without knowledge of the mechanistic pathway.

As modifying terms in regiospecific addition reactions the indication of two vicinal groups in the product (one derived from the reagent and one from the unsaturated substrate—in that order) is proposed. Thus eq 3 shows Br–phenyl regiospecificity and eq 4 shows H–carbonyl[7] regiospecificity.

Further illustrations are given by the S–H regiospecific nucleophilic addition of thioalkoxide to acetylenes[8] (eq 5), the Br–phenyl regiospecific free-radical addition of bromine azide[3] (eq 6), and the H–CH$_3$ regiospecific hydroboration of methylcyclohexene[9] (eq 7).

$$C_6H_5C{\equiv}CH + CH_3SNa \longrightarrow C_6H_5CH{=}CHSCH_3 \quad (5)$$

$$C_6H_5CH{=}CH_2 + BrN_3 \xrightarrow{N_3 \cdot} C_6H_5CHCH_2N_3 \quad (6)$$
$$\underset{\displaystyle Br}{|}$$

The advantage of this convention is that mechanistic interpretations can be added if desired. Thus, the N$_3$-butyl regiospecificity in IN$_3$ addition to 1-hexene[10] (eq 8) is attributable to electronic factors whereas the I-*t*-butyl regiospecificity[11] in eq 9 is sterically controlled (and may be termed sterically regiospecific).

$$n\text{-Bu}{-}CH{=}CH_2 + IN_3 \longrightarrow n\text{-Bu}{-}\underset{\displaystyle N_3}{\underset{|}{CH}}{-}\underset{\displaystyle I}{\underset{|}{CH_2}} \quad (8)$$

$$t\text{-Bu}{-}CH{=}CHCH_3 + IN_3 \longrightarrow t\text{-Bu}{-}\underset{\displaystyle I}{\underset{|}{CH}}{-}\underset{\displaystyle N_3}{\underset{|}{CHCH_3}} \quad (9)$$
$$\mathbf{1}$$

This terminology can also be used profitably in elimination reactions. Thus, if elimination of HBr from 2 occurs preferentially in one of the two possible directions,[12] the reaction is said to be regioselective.

For such reactions we prefer the well-established modifying terms *Saytzeff* and *Hofmann*.[13] If elimination of HX proceeds in the direction of the more substituted olefin, the reaction may be said to be Saytzeff regiospecific. Preferential elimination to the less substituted olefin, *e.g.*, eq 10, is Hofmann regioselective.
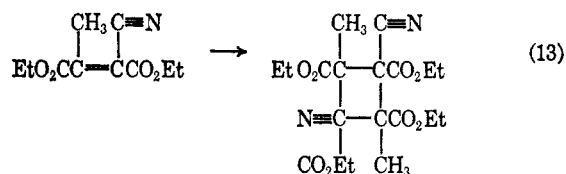
$$CH_3CH_2C{=}CH_2 + CH_3CH{=}CCH_3 \quad (10)$$
$$72\% \qquad\qquad 28\%$$
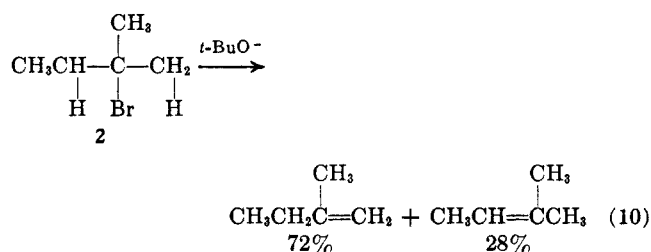
The concept of regiospecificity can be usefully employed in an even wider sense. Unique modifying terms can be used in describing particular reactions, some examples of which follow.

Reactions of ambident ions can be described in this context. Thus, eq 11 is a C-regiospecific alkylation, while 12 is O regioselective.[14] Using inorganic ions as an example, the displacement of alkyl halides with nitrite ion can be N over O regioselective.[15]

main product
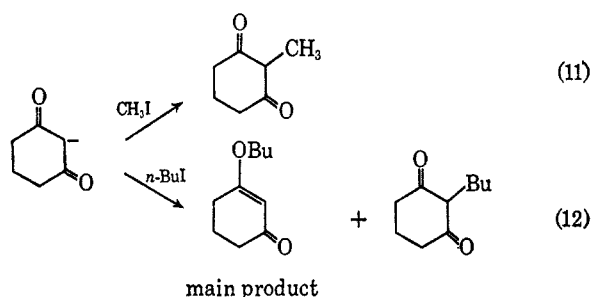
Cycloadditions, dimerizations, 1,3-dipolar additions, and Diels–Alder reactions can be regiospecific or regioselective. Equation 13 is an example of a nonvicinally regiospecific dimerization.[16] Diels–Alder reactions usually are vicinally regioselective[17] (eq 14). The term vicinal is to be employed when the two identical groups or the two largest groups originally on separate molecules are found in the closest of the two possible positions in the product. Additional clarification may be

(6) M. M. Maire, *Bull. Chem. Soc. Fr.*, [4] **3**, 281 (1908).

(7) Br–H regiospecificity is equally valid.

(8) W. E. Truce and J. A. Simms, *J. Amer. Chem. Soc.*, **78**, 2756 (1956).

(9) H. C. Brown, "Hydroboration," W. A. Benjamin Inc., New York, N. Y., 1962.

(10) F. W. Fowler, A. Hassner, and L. A. Levy, *J. Amer. Chem. Soc.*, **89**, 2077 (1967).

(11) A. Hassner and F. W. Fowler, *J. Org. Chem.*, **33**, 2686 (1968).

(12) H. C. Brown and I. Montani, *J. Amer. Chem. Soc.*, **75**, 4112 (1953).

(13) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953; J. S. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co. Inc., New York, N. Y., 1956; E. S. Gould, "Mechanism and Structure in Organic Chemistry," H. Holt and Co., New York, N. Y., 1959.

(14) H. Stetter and W. Dierichs, *Ber.*, **85**, 61 (1952).

(15) N. Kornblum, R. A. Smiley, and R. B. Blackwood, *J. Amer. Chem. Soc.*, **77**, 6269 (1955).
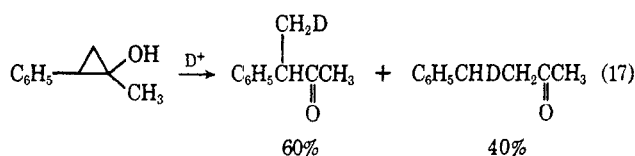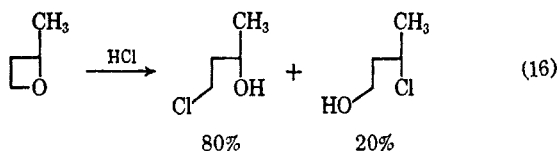
(16) C. K. Ingold, E. A. Perren, and J. F. Thorpe, *J. Chem. Soc.*, **121**, 1765 (1922).

(17) R. Huisgen, R. Grashey, and J. Souer, "The Chemistry of Alkenes," S. Patai, Ed., Interscience Publishers, Inc., London, 1964, Chapter 11, p 915.

required on occasion as for the phenyl–propyl nonvicinally regiospecific dipolar addition shown in eq 15[18] below.

(14)

(15)
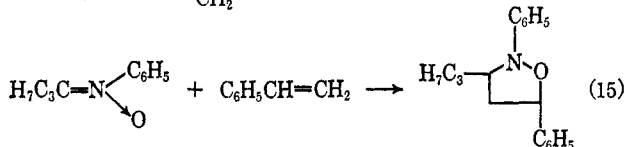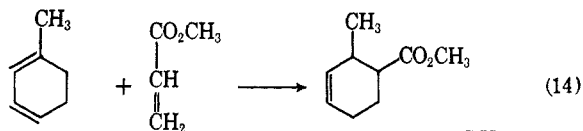
Ring-opening reactions of heterocycles such as aziridines, epoxides, larger ring ethers, lactams, and lactones as well as of other ring compounds can occur in a regiospecific or selective manner, i.e., the Cl–H over Cl–CH₃ regioselective opening of oxetanes (eq 16)[19] and the D–H over D–phenyl regioselectivity in the opening of cyclopropanols[20] (eq 17).

(16)

(17)

Hydride opening of 6β,7β-epoxycholestane is H–(C-7) regiospecific, consistent with diaxial opening of epoxides[21] (eq 18).

(18)

Electrophilic, nucleophilic, or free-radical aromatic substitutions may be *ortho, meta,* or *para* regioselective.

In inorganic chemistry examples of regioselective reactions can be found among others in alkylations[22] or deuterium exchange[23] involving decaboranes and halogenation of B₅H₉.[24]

Finally the concept can be applied to positional isomerism, so that 3 and 4 can be termed regioisomers (synonymous with position isomers).[25]
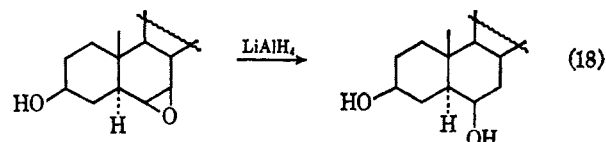
(18) R. Grashey, R. Huisgen, and H. Leitermann, *Tetrahedron Lett.*, 9 (1960).
(19) S. Searles, K. A. Pollart, and F. Blaock, *J. Amer. Chem. Soc.*, **79**, 952 (1957).
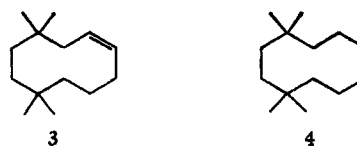(20) C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, *ibid.*, **88**, 3347 (1966).

(21) E. J. Corey, *ibid.*, **76**, 175 (1954).
(22) I. Dunston, R. C. Williams, and N. J. Blay, *J. Chem. Soc.*, 5012 (1960).
(23) J. A. Dupont and M. F. Hawthorne, *J. Amer. Chem. Soc.*, **84**, 1804 (1962).
(24) R. Schaeffer, J. N. Shoolery, and R. Jones, *ibid.*, **80**, 2670 (1958).
(25) M. Svoboda, J. Zavada, and J. Sicher, *Collect. Cvech. Chem. Commun.*, **32**, 2104 (1967).

A General Synthesis of Vinyl Azides from Olefins. Stereochemistry of Elimination from β-Iodo Azides[1a]

ALFRED HASSNER AND FRANK W. FOWLER[1b]

Department of Chemistry, University of Colorado, Boulder, Colorado 80302

Treatment with base of β-iodo azides, prepared by the addition of iodine azide to olefins, resulted generally in vinyl azides, suggesting a directive effect of the azido function. Terminal olefins, vicinally disubstituted olefins, and unsaturated carbonyl compounds all led regiospecifically to the vinyl azides. Indene, 1,2-dihydronaphthalane, cyclooctene, and 1,3-cyclooctadiene also gave the vinyl azides. However, the iodine azide adducts of cyclopentene and cyclohexene produced the allyl azides. Apparently, the stereoelectronic preference for *trans* elimination is greater than the directive effect of the azido function. An assignment of *cis* configuration to the double bond in the eight-membered-ring vinyl azides, made on the basis of nmr data, suggests *syn* elimination of hydrogen iodide in these systems. Regioselectivity in IN₃ additions to olefins is discussed.

The simplest vinyl azide, azidoethylene, was prepared by Forster and Newman[2] as early as 1910. However, since then very few vinyl azides have been reported[3] and, although some have been found to be

valuable intermediates for the synthesis of 1-azirines,[4] their chemistry has not been explored very extensively. Consequently a general synthesis of vinyl azides (Table I) would be desirable for it should allow for the investigation of this relatively unknown class of com-

(1) (a) Stereochemistry. XXXV. For paper XXXIV, see A. Hassner, *J. Org. Chem.*, **33**, 2684 (1968). (b) NASA Predoctoral Fellow, 1965–1967.
(2) M. O. Forster and S. H. Newman, *J. Chem. Soc.*, **97**, 2570 (1910).
(3) (a) J. H. Boyer and F. C. Cantes, *Chem. Rev.*, **54**, 1 (1954); (b) E. Lieber, J. S. Curtice, and C. N. R. Rao, *Chem. Ind.* (London), 586 (1966).

(4) (a) G. Smolinsky, *J. Amer. Chem. Soc.*, **83**, 4483 (1961); (b) G. Smolinsky, *J. Org. Chem.*, **27**, 3557 (1962); (c) A. Hassner and F. W. Fowler, *J. Amer. Chem. Soc.*, **90**, 2875 (1968).