



# Science of Synthesis

Houben-Weyl Methods of Molecular Transformations

*Editorial Description*



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# 1 Editorial Description of Science of Synthesis

## 1.1 Why is there a Need for a New Edition of Houben–Weyl Methods of Organic Chemistry?

Synthesis is seen as the cornerstone of drug discovery; as John L. LaMattina, Vice President for Discovery Research at Pfizer stated, “You need to get in the lab and make compounds and convert these compounds to drugs. That is a chemistry-intensive step.” (*Chemical and Engineering News*, March 1998). Thus chemists today are facing ever-increasing demands on their time and synthetic excellence, whilst pharmaceutical and chemical companies are recognizing the need to move towards developing more efficient and productive R & D laboratories. Just to maintain current growth rates of 10% a year, the top ten pharmaceutical companies would each have to launch five new drugs a year.

One of the key challenges facing these companies and scientists in academia is information management: the amount of chemical literature available from journals, and on-line and CD-ROM databases, has grown exponentially. Researchers today are facing ‘information overload’ on reaction schemes and synthetic routes, even though a large number of products made in industry today are being produced with traditional synthetic methods developed 40 to 50 years ago.

With this in mind, Thieme Publishers has seen the need to relaunch the *Houben–Weyl* series, a classical reference work in organic chemistry, in a new, very accessible, and focused format called **Science of Synthesis, Houben–Weyl Methods of Molecular Transformations**. By providing a clear and systematic synthesis series, **Science of Synthesis** is designed to be the first point of reference before embarking on further searches, providing a route through the mass of information available in the primary literature. **Science of Synthesis** contains synthetic methods selected by world-renowned chemists, giving full experimental procedures and background information.

**Science of Synthesis** is designed to stimulate new discoveries and the development of new methodologies in both industry and academia by providing an understanding of the whole field of synthesis to date.

**Science of Synthesis** is a flexible user-friendly system, allowing text, substructure, exact structure, and reaction searches with an easy-to-use interface.

**Science of Synthesis** is an expert guidance tool giving high-quality, reliable, and selective solutions to scientists’ synthesis problems.

## 1.2 Houben–Weyl Methods of Organic Chemistry Entering the New Millennium

The series *METHODEN DER ORGANISCHEN CHEMIE (Houben–Weyl Methods of Organic Chemistry)* was established in 1909 by the German chemist Theodor Weyl and continued in 1913 by Heinrich J. Houben. The comprehensive description of preparative methods in a consistent style and their critical evaluation by leading experts is the philosophy on which *Houben–Weyl* was founded. The 4 volumes of the second edition were published between 1921 and 1924. The third edition, consisting of 4 volumes, was published between 1924 and 1941. The fourth edition (founded by O. Bayer, H. Meerwein, E. Müller, K. Ziegler) began in 1952, was continued from 1975 by H. Kropf and H.-G. Padeken, and ended in 1986 with a total of 67 volumes and 3 index volumes. The series was updated with 89 additional and supplementary volumes which placed emphasis on the treatment of important classes of compounds and significant preparative methods (edited by K. H. Büchel, J. Falbe, H. Hagemann, M. Hanack, D. Klamann, R. Kreher, H. Kropf, M. Regitz, E. Schaumann, and H.-G. Padeken). From 1990 onwards *Houben–Weyl* was published in English, thus making it accessible to chemists worldwide. The last volume of *Houben–Weyl* was published in the year 2003. The appendix contains a list of all *Houben–Weyl* volumes.

The success of *Houben–Weyl* over the last 90 years was made possible by the collaborative work of world-renowned chemists in both industry and academia, who created a balanced work by considering published results from journals, books, and the patent literature. Thus, *Houben–Weyl* has become an important and celebrated standard reference work, serving the scientific community with a critical selection of synthetic methods. *Houben–Weyl* is an indispensable treatise for every synthetic chemist.

At the turn of the century *Houben–Weyl* is now heading towards new directions. Facing dramatic developments in organic chemistry during the last decades, which have provided synthetic chemists with a wealth of new reagents and reactions, the board of editors has decided to carry on the long tradition of *Houben–Weyl*. An entirely new edition of *Houben–Weyl* has been launched in the year 2000. This new edition is entitled **Science of Synthesis, Houben–Weyl Methods of Molecular Transformations** and is edited by D. Bellus (Basel, Switzerland), E. N. Jacobsen (Cambridge, USA), S. V. Ley (Cambridge, UK), R. Noyori (Nagoya, Japan), M. Regitz (Kaiserslautern, Germany), P. J. Reider (New Jersey, USA), E. Schaumann (Clausthal-Zellerfeld, Germany), I. Shinkai (Tsukuba, Japan), E. J. Thomas (Manchester, UK), and B. M. Trost (Stanford, USA). **Science of Synthesis** will benefit from more than 90 years of experience and will continue the tradition of excellence in publishing organic chemistry reference works. It will offer a truly comprehensive, critical treatment of synthetic organic and organometallic chemistry. **Science of Synthesis** will cover the whole field of organic chemistry based on all published and readily available sources from the early 1800s until the year of publication. Widely acclaimed editors and authors will provide chemists with the most reliable methods to solve their synthesis problems. For each method a detailed experimental procedure will be included. **Science of Synthesis** will be updated periodically and will become a prime source of information for scientists in the 21st century.

To best meet the needs of the scientific community, **Science of Synthesis** is published not only in a print version but also as an electronic version, which makes use of the latest developments in information technology and is equipped with a powerful and user-friendly information-retrieval system to allow for substructure, exact structure, and reaction searches. The electronic version is being developed under the guidance of an advisory board comprising A. Barth (Fachinformationszentrum Karlsruhe, Germany), G. Baysinger (Stanford University, USA), A. Mullen (Bayer AG, Germany), H. Rzepa (Imperial College, UK), and E. Zass (ETH Zürich, Switzerland). **Science of Synthesis** will support combined keyword, text and reaction searches. It will provide a hypertext navigation system and thesaurus support. Crossovers to databases and electronic journals are fully supported, thus allowing chemists to gather further information about their target compounds. Chemists are provided with customizable display and print formats. **Science of Synthesis** will be at the heart of the fully integrated laboratory of the future.

The policy of the editorial board and the publishers is to ensure that **Science of Synthesis** is the ultimate tool for the synthetic chemist in the 21st century. This endeavor will be achieved by the combined efforts of the publishing house, the editors, and the authors, who are among the leading experts in their field.

### 1.3 Organizational Principles of Science of Synthesis, Houben–Weyl Methods of Molecular Transformations

The following organizational principles are designed to serve as guidelines for volume editors, authors, and users in deciding where in **Science of Synthesis** a given topic will be treated. These rules of classification will not, however, take precedence over chemical common sense in the organization of individual volumes, since it is the ultimate goal that the material be organized for the benefit of the user in a manner that is as simple and intuitive as possible.

### 1.3.1 Classification Principles

The organization of **Science of Synthesis** is based on the structural unit or functional group (for example, a heteroaromatic ring or an enone) that is to be constructed. That is to say **the classification is based on the product** (how do I make something?) as opposed to the reaction (what is the Horner–Emmons reaction?), the reagent (what can I do with organocopper reagents?), or the starting material (what reactions do 1,2-diols undergo?). Thus, a given synthetic method, such as catalytic hydrogenation, that can be employed for a variety of product types, will be found throughout the work, depending on the structure of the compound produced. Likewise, the various reactions of a given compound class, such as alcohols, are located throughout the work on the basis of the product.

The purpose of this classification system is to organize all synthetically useful reactions so that practicing chemists can readily find a solution to their synthetic problem, and ensure a minimum of overlap in the presentation throughout the entire work. Unfortunately, there is no universal organizational principle for all organic and organometallic chemistry that is simple and at the same time corresponds to generally accepted chemical common sense. Therefore, the following rules have not been rigorously derived from physical or chemical principles.

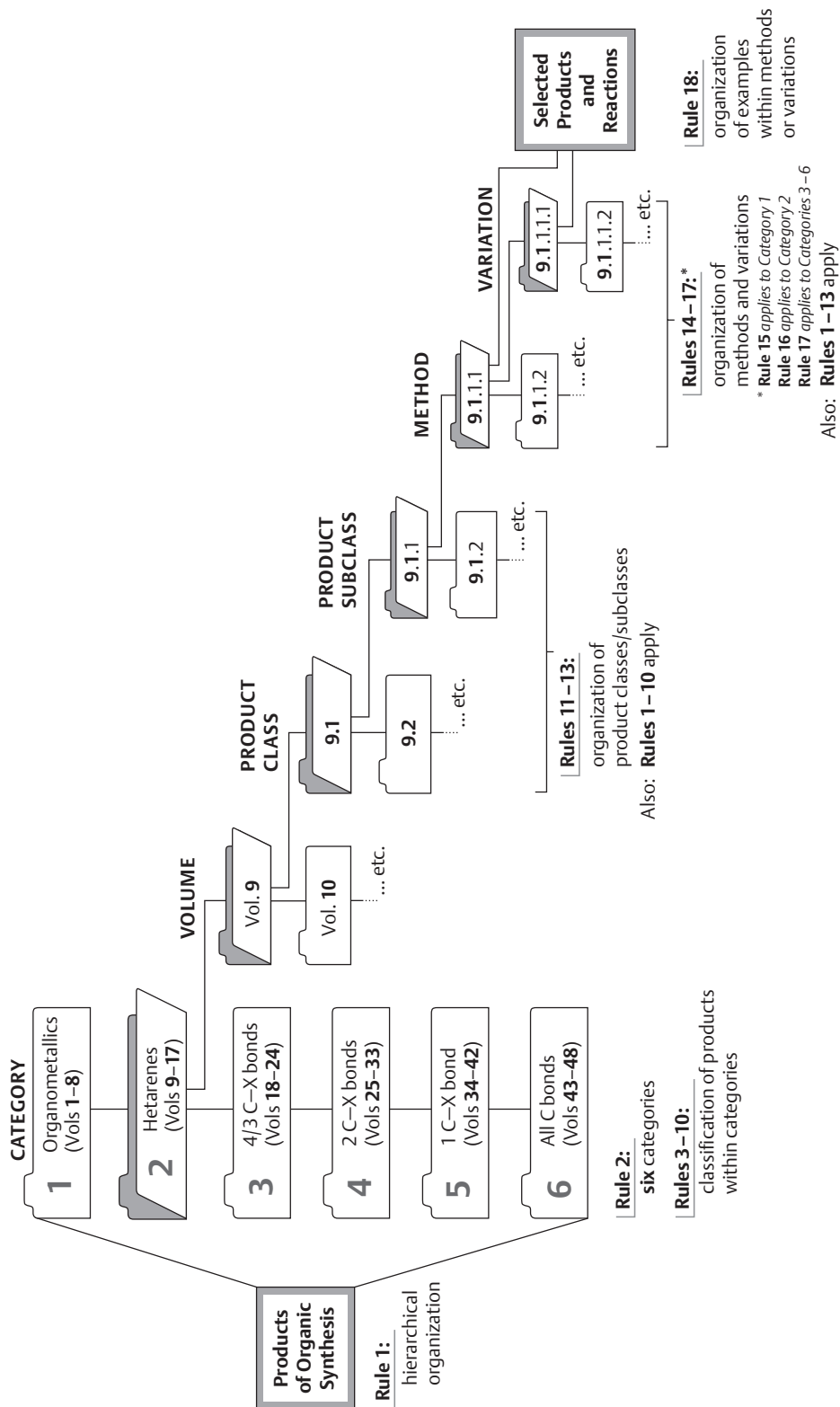
A classification scheme is employed that corresponds to the general notion of oxidation state (carbonic acid derivatives, carboxylic acid derivatives, etc.). It is of interest to note that the number of heteroatom bonds to carbon, which is a rough indication of oxidation state, has been the underlying organizational principle of *Houben–Weyl* since the first edition. For organometallic and heteroaromatic compounds the editors have created two separate categories, in accordance with common chemical usage and the fact that these compound classes have unique chemical properties. Partially or fully saturated heterocyclics are, however, classified with the corresponding acyclic compounds (e.g., tetrahydrofuran with ethers).

The result is a group of six categories given below in Section 1.3.1.2. When only one functionality is present in the target, the classification into one of the six categories is evident. This is also true with targets containing mutually remote functionalities in which only one functionality is formed by the method under consideration, since the classification is based solely on the functionality formed. However, with multifunctional targets, in which functionalities are directly bonded or in which more than one functionality is formed by the method under consideration, more elaborate classification rules are needed in order to determine in which category the target belongs and where within the category it will be treated (for an overview see Scheme 1). As with the Cahn–Ingold–Prelog system, all functional groups and structural units must be given an order of priority for the purposes of classification. In each case where multiple functions are formed at the same time, the decision has to be made as to which functional group has the higher priority. For example, is the lithiation of pyridine covered under organometallics or heteroarenes, i.e. which functionality has the higher priority, C–Li or pyridine? The following rules attempt to answer all such questions.

Scheme 1 gives an overview of the classification principles of **Science of Synthesis**.

Scheme 1

Classification Principles of Science of Synthesis (Volume 9 Given as an Example)



### 1.3.1.1 **Modular Organization of the Text of Science of Synthesis**

#### **Rule 1 Hierarchical Organization of the Content of Science of Synthesis**

The content of **Science of Synthesis** will be organized hierarchically into:

- Categories,
- Volumes,
- Product Classes,
- Product Subclasses,
- Methods,
- Variations.

Each product class can be divided into product subclasses if necessary. Methods will be ranked according to the organizational principles (e.g., in the case of allylstannanes, the synthesis of these products by formation of the C–Sn bond via a Grignard reaction has a higher priority than the synthesis by formation of the allylic C=C bond via a Wittig reaction, see Rule 14). **Science of Synthesis** will focus on selected and reliable methods, which have proved to be useful for the synthesis of a given product class. For each method a scheme and, if necessary, a table (with, in general, 5 to 10 examples) will be given. An experimental procedure, plus safety and environmental aspects, will further illustrate the method. Alterations to a method, e.g. changes in catalysts or reagents, the running of a reaction as a one-pot reaction, generation of reagents in situ, etc., which have a significant influence on the outcome of a reaction, will result in a variation. A variation will be described in the same way as a method. If there are several variations of a method, Method *n* as a heading (with introductory text only) is followed by Variation 1 (including introductory text, scheme, table of examples, experimental procedure), Variation 2, etc.

According to these principles the text will be organized into the following sections:

#### **Category 1**

- 1** Volume 1
  - Introductory Text: Volume 1
    - Background Information: Products of Volume 1 (e.g., history, nomenclature, applications)
    - Structure: Products of Volume 1
    - Stability: Products of Volume 1
    - Reactivity: Products of Volume 1
    - Physical Properties: Products of Volume 1
    - Spectroscopic Properties: Products of Volume 1
    - Safety and Environmental Aspects: Products of Volume 1
- 1.1** **Product Class 1** (based on the organizational principles of **Science of Synthesis**)
  - Introductory Text: Product Class 1
    - Background Information: Product Class 1 (e.g., history, nomenclature, applications)
    - **Location of Product Class 1 in Houben–Weyl, 4th Edition and E-Series**
    - Structure: Product Class 1
    - Stability: Product Class 1
    - Reactivity: Product Class 1
    - Physical Properties: Product Class 1
    - Spectroscopic Properties: Product Class 1
    - Safety and Environmental Aspects: Product Class 1

- 1.1.1    **Product Subclass 1**
  - Introductory Text: Product Subclass 1
  - Background Information (e.g., history)
  - Comparison of Methods
  - Mechanistic Rationale
  - Stereochemistry
  - Scope
  - Limitations and Problems
  - Functional Group Compatibility
  - Safety and Environmental Aspects
- 1.1.1.1    **Method 1**
  - Introductory Text: Method 1
  - Background Information: Method 1 (e.g., history)
  - Mechanistic Rationale
  - Stereochemistry
  - Scope
  - Limitations and Problems
  - Functional Group CompatibilityMethod 1: Scheme  
Method 1: Table of Examples  
Method 1: Experimental Procedure  
Method 1: Safety and Environmental Aspects
- 1.1.1.1.1    **Variation 1**
  - Introductory Text: Variation
  - Background Information: Variation 1 (e.g., history)
  - Mechanistic Rationale
  - Stereochemistry
  - Scope
  - Limitations and Problems
  - Functional Group CompatibilityVariation 1: Scheme  
Variation 1: Table of Examples  
Variation 1: Experimental Procedure  
Variation 1: Safety and Environmental Aspects
- 1.1.1.1.2    **Variation 2**
- 1.1.1.1.*n*    **Variation *n***
- 1.1.1.2    **Method 2**
- 1.1.1.2.1    **Variation 1**
- 1.1.1.2.*n*    **Variation *n***
- 1.1.1.*n*    **Method *n***
- 1.1.2    **Product Subclass 2**
- 1.1.*n*    **Product Subclass *n***
- 1.2    **Product Class 2**
- 1.*n*    **Product Class *n***
- 2    **Volume 2**
- n*    **Volume *n***
- Category 2**
- n* + 1    **Volume *n* + 1**
- Category *n***
- Category 6**

### 1.3.1.2 Classification of Products into Compound Categories

#### Rule 2 Categories

All organic compounds are organized into six categories:

- Category 1: *Organometallics,*
- Category 2: *Heteroarenes and Related Ring Systems,*
- Category 3: *Four and Three Carbon–Heteroatom Bonds,*
- Category 4: *Two Carbon–Heteroatom Bonds,*
- Category 5: *One Carbon–Heteroatom Bond,*
- Category 6: *All-Carbon Functions.*

The priority among the categories corresponds to their order, with organometallics at the top. Category 1 focuses on organometallic and other metal-containing species which are important for synthetic transformations. The assignment of a functional group to Categories 3–5 is determined by the highest number of carbon–heteroatom (C–X) bonds to a single carbon atom, which can be either the carbon atom of attachment (e.g., C–OH, Category 5) or one in the functional group (e.g., CO<sub>2</sub>H, Category 3). This corresponds roughly to the standard classification by oxidation state into carbonic acid derivatives, carboxylic acid derivatives, ketone derivatives, etc.

*Example:* Compounds with a carbon–metal bond formed are treated in Category 1. Organic compounds with a heteroatom–metal bond formed, however, are treated in Categories 2–5 with the corresponding heteroatom functional group; carboxylates, enolates and alcoholates, for example, are covered in Categories 3, 4 and 5, respectively.

### 1.3.1.3 General Rules for the Classification of Products within Categories

#### Rule 3 Isolable Products

In general, only isolable products are included in the organizational scheme; intermediates are dealt with under mechanistic considerations for individual synthetic methods. Exceptions are key organometallic intermediates in reactions that form a metal-free product and important reactive intermediates that are formed in situ (e.g., some ylides and ketenes).

#### Rule 4 Heteroatoms

For the purposes of classification in **Science of Synthesis**, the following elements are considered to be “heteroatoms”: F, Cl, Br, I, O, S, Se, Te, N, P (Scheme 2).

All other elements (except C and H) are classified as metals and their compounds with carbon are found in Category 1 (note that B, Si and As are classified with the metals).

## Scheme 2

1																	18
1 H												2 He					
3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg	3	4	5	6	7	8	9	10	11	12	13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
55 Cs	56 Ba	57 # La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
87 Fr	88 Ra	89 § Ac	104 Unq	105 Unp	106 Unh												

# Lanthanide Series

58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu
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§ Actinide Series

90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr
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**Rule 5 Multifunctional Compounds**

In multifunctional compounds, the functional group produced by a given method determines the location of that compound in **Science of Synthesis**; other remote functional groups within this compound that remain unchanged are neglected in the classification, even if they have a higher priority.

*Exception:* See Rule 10 below for the geminal attachment of two functional groups to one carbon.

**Rule 6 Two or More Functional Groups**

When two or more functional groups are produced at the same time, the assignment to one of the six categories is determined by the functional group with the highest priority.

**Rule 7 C–X and C–C  $\pi$ -Bonds**

Functional groups containing C–X and C–C  $\pi$ -bonds (e.g., C=C–X) are classified according to the highest number of both of these types of bonds to a single carbon atom, i.e. the C–C  $\pi$ -bond is treated as an additional C–X bond.

*Example:* Enol derivatives are found in the same category as ketones (Category 4). 1,2-Dihaloalkenes (X–C=C–X) are also found in Category 4, while 1,1,2-trihaloalkenes (X–C=CX<sub>2</sub>) are found in Category 3.

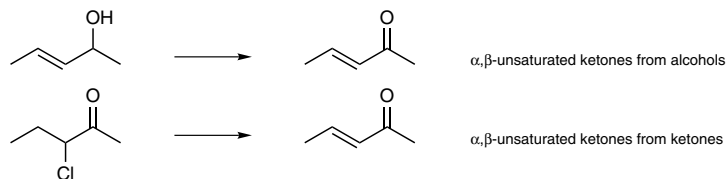
Within a category, the true C–X bond takes precedence over the C–C  $\pi$ -bond, e.g. CX<sub>2</sub> > C=C–X within Category 4 (see Rule 12).

**Rule 8 Extended  $\pi$ -Conjugation**

Structural units with extended  $\pi$ -conjugation are considered as a single functional group and are usually treated in a separate section (Scheme 3).

*Example:* Syntheses of  $\alpha,\beta$ -unsaturated ketones are found in Category 4, regardless of which part of the structural unit is produced by the method.

Scheme 3



### Rule 9 Conjugated Functional Group

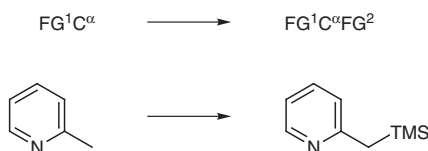
When a conjugated functional group reacts, the classification is determined by the functional group in the product with the higher priority.

*Example:* The reduction of the C=C bond of an  $\alpha,\beta$ -unsaturated ketone is covered under “ketones from  $\alpha,\beta$ -unsaturated ketones” and not under “alkanes from alkenes”.

### Rule 10 The $\alpha$ -Rule

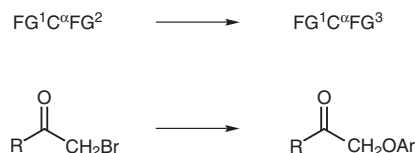
For reactions at the carbon  $\alpha$  to a  $\pi$ -functional group (FG<sup>1</sup>, e.g., arene, heteroarene, CO<sub>2</sub>H, C=O, C≡N, C=C, Scheme 4) resulting in the formation of any second functional group (FG<sup>2</sup>, e.g., OH, SR)

Scheme 4



or transforming a second functional group (FG<sup>2</sup>, Scheme 5),

Scheme 5



the choice of higher priority between FG<sup>1</sup> and FG<sup>2</sup> or between FG<sup>1</sup> and FG<sup>3</sup> in the product determines the classification. In Scheme 4, silicon has the higher priority, while in Scheme 5 the ketone has the higher priority.

*Example:* All reactions  $\alpha$  to a heteroaromatic ring, except the formation of a C–M product, are found in Category 2 with the heteroarene under consideration. Monohalogenation of ketones is covered under ketones (Category 4), not under halides (Category 5), while  $\alpha$ -alkoxycarbonylation of ketones is covered under esters (Category 3). Syntheses of allylic and benzylic alcohols are covered with alcohols in Category 5.

### 1.3.1.4 Product Classes within the Categories

The organization within the six categories is based on the following priority rules:

#### Rule 11 Priority Among Elements

All metals have a higher priority than all heteroatoms (see Rule 4). With this in mind, the groups of elements of the periodic table have decreasing priority from right to left and then within each group decreasing priority from top to bottom.

*Example:* O > S > Se > N > P

#### Rule 12 Priority Among Functional Groups

Priority among functional groups is determined firstly by the highest number of true C–X (or C–M) bonds to a single carbon atom and secondly by the highest number of  $\pi$ -bonds to a single carbon atom (i.e.,  $sp > sp^2 > sp^3$ ). If two functional groups are equal according to the above, further carbon atoms in the functional groups are compared until a difference is found.

*Example:* C=X > C=C–X and C $\equiv$ X > C $\equiv$ C–X (more true C–X bonds to one carbon); C $\equiv$ X > CX<sub>3</sub> (hybridization); X–C=C–X > C=C–X (number of C–X bonds to further carbon atoms); C=C–C=C > C=C and C $\equiv$ C > C=C=C (hybridization of further carbon atoms).

#### Rule 13 Priority for a Carbon-Bound Heteroatom

The priority for a carbon-bound heteroatom X is generally determined by the sequence –X–H > –X–M (metal priorities as above) > –X–C > –X–Y (priorities of heteroatoms Y as above) and the oxidation state of heteroatom X. The order in specific volumes, however, may deviate from this rule, based on the nature of the compound class under consideration. Therefore, the tables of contents of the individual volumes covering organosulfur, organonitrogen, and organophosphorus compounds should be referred to.

*Example:* ROH > ROM > ROR > ROOH and R–SO<sub>3</sub>–H > R–SO<sub>2</sub>–H > RSOH.

### 1.3.1.5 Methods and Variations within the Product Classes

#### Rule 14 Organization of Methods and Variations

Methods and variations within a given product class or product subclass are organized where applicable in the hierarchical fashion presented below (**x**: volume, **y**: product class, **z**: product subclass). The headings/subheadings are guidelines for the organization of the various methods, and need not be adopted verbatim in the text. For the purpose of prioritizing reactions involving more than one component (e.g., exchange and addition reactions), the component which is to be modified is defined as the one containing the functional group belonging to the product class **y**, irrespective of the priority of other groups involved (actively or passively) in the transformation. For methods which in most respects are similar (e.g., substitution reactions involving the transformation of identical highest priority components), chemical common sense should take precedence and further ordering is left to the discretion of the author and/or volume editor.

#### Synthesis by Substitution

- x.y.z.1** Of Hydrogen  
(includes oxidation C–H → C–OH)
- x.y.z.2** Of Organometallic Groups

- x.y.z.3** Of Carbon Functionalities  
(if two functionalities are involved, the one of highest rank decides)
- x.y.z.4** Of Heteroatoms

#### **Synthesis by Elimination**

- x.y.z.5** Of Hydrogen  
Priority: (1) H<sub>2</sub>, (2) H–M, (3) H–R, (4) H–X
- x.y.z.6** Of Organometallic Groups  
(M–C or M–X)
- x.y.z.7** Of Carbon Functionalities
- x.y.z.8** Of Heteroatoms  
(includes Wittig reaction)

#### **Synthesis by Addition Reactions**

- (includes C–C cleavage)
- x.y.z.9** Of Hydrogen  
Priority: (1) H<sub>2</sub>, (2) H–M, (3) H–R, (4) H–X
- x.y.z.10** Of Organometallic Groups  
(M–C or M–X)
- x.y.z.11** Of Carbon Functionalities
- x.y.z.12** Of Heteroatoms  
(includes carbonyl → acetal)

- x.y.z.13** **Synthesis by Rearrangement**

- x.y.z.14** **Synthesis with Retention of the Functional Group**  
(e.g., introduction or elimination of a second group, chain elongation, transesterification)

### **Rule 15 Organization of Methods and Variations within Category 1**

The following points should be taken into consideration when preparing a manuscript for the organometallics category.

**Product Class:** For each metal there will be a separate product class. However, transition metals with closely related chemistry can be described in one product class to avoid redundancy of the methods described. The introductory texts for each product class should include problems of preparation, stability, and reactivity and be followed by a discussion on the scope of the reactions which employ the described product class, utility/versatility in organic synthesis, and whether the reaction is catalytic or stoichiometric.

**Product Subclass:** Product classes will be divided into product subclasses depending on the ligands of the metal. Product subclasses should be ordered with descending hapticity of the ligands. Charged complexes should be ordered within product subclasses as follows: (1) neutral, (2) anionic, (3) radical anion, (4) radical, (5) radical cation, (6) cationic. It is recognized that the concept of charge of an organometallic species can in some cases only be applied to the extent possible, i.e. for defined conditions (e.g., for a defined polarity of the solvents).

The oxidation state of the metal should be used for the description of the product subclasses.

For each product subclass two aspects can be described: **Synthesis of the Product Subclass** and **Applications of the Product Subclass in Organic Synthesis**. For similar treatment within Categories 3–6, see Rule 17.

**Synthesis of the Product Subclass:** Methods should be organized according to the organizational principles described in Rule 14.

**Applications of the Product Subclass in Organic Synthesis:** In this section typical methods for the use of the product subclass in organic synthesis can be described, if the product subclass in question is synthetically important. Reactions involving catalytic amounts of an organometallic complex or an uncharacterized intermediate should be given as methods. These methods usually give products that belong to other product classes within different categories of **Science of Synthesis**. These other product classes will also be discussed extensively in the appropriate category of **Science of Synthesis**, but in the organometallics category emphasis will be placed on the role of the organometallic complex. The organometallic volumes also contain inorganic compounds, metal compounds without a formal metal–carbon bond, that are significant for synthetic chemistry. The inorganic compound is conveniently covered together with true organometallics of similar structure (e.g.,  $\text{AlH}_3$  with  $\text{R}_2\text{AlH}$ ). For those compounds that are readily available commercially, methods for their synthesis can be neglected such that only methods for their applications in organic synthesis are included. To the extent that an inorganic reagent is used mainly for metalation, then the principal treatment will come under the organometallic intermediate: its synthesis (using the inorganic reagent) and its further applications in organic synthesis.

**Ranking of applied methods** should be carried out:

1. according to Rule 14 (preferred)
2. according to the product group being discussed  
(e.g., see **Science of Synthesis**, Volume 4, Section 4.4.12:
  - 4.4.12 Product Subclass 12: Haloorganosilanes...  
Applications of Product Subclass 12 in Organic Synthesis
  - 4.4.12.9 Fluoroorganosilanes
  - 4.4.12.10 Chloroorganosilanes
  - 4.4.12.11 Bromoorganosilanes
  - 4.4.12.12 Iodoorganosilanes)
3. according to the product produced (see Section 1.3.1.3 and Section 1.3.1.4)

An example of this would be the synthesis of dialkylzinc compounds and the use of dialkylzinc compounds in the synthesis of secondary alcohols. In **Science of Synthesis** this would be dealt within the organometallics category as follows:

<b>Category 1:</b>	Organometallics
<b>Volume 3:</b>	Compounds of Groups 12 and 11 (Zn, Cd, Hg, Cu, Ag, Au)
<b>Product Class:</b>	Organometallic Complexes of Zinc
<b>Product Subclass:</b>	Metal $\sigma$ -Alkyl Homoleptic Complexes <i>Synthesis of Product Subclass:</i>
<b>Method x:</b>	Synthesis of Dialkylzinc Compounds <i>Applications of Product Subclass in Organic Synthesis:</i>
<b>Method x:</b>	Synthesis of Secondary Alcohols Using Dialkylzinc Compounds

There would also be a duplicate entry present in the one carbon–heteroatom bond category as follows:

<b>Category 5:</b>	Compounds with One Carbon–Heteroatom Bond
<b>Volume 36:</b>	Alcohols
<b>Product Class:</b>	Secondary Alcohols
<b>Method x:</b>	Synthesis of Secondary Alcohols Using Transition Metals

The **table of contents** should take the following format:

	<b>Category 1: Organometallics</b>
<b>x</b>	<b>Volume X</b>
<b>x.y</b>	<b>Product Class Y: Organometallic Complexes of Metal X</b>
<b>x.y.1</b>	<b>Product Subclass 1: Metal–Arene Complexes</b> <i>Synthesis of Product Subclass 1</i>
<b>x.y.1.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 1 in Organic Synthesis</i>
<b>x.y.1.n</b>	<b>Method n</b>
<b>x.y.2</b>	<b>Product Subclass 2: Metal–Triene Complexes</b> <i>Synthesis of Product Subclass 2</i>
<b>x.y.2.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 2 in Organic Synthesis</i>
<b>x.y.2.n</b>	<b>Method n</b>
<b>x.y.3</b>	<b>Product Subclass 3: Metal–Dienyl Complexes</b> <i>Synthesis of Product Subclass 3</i>
<b>x.y.3.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 3 in Organic Synthesis</i>
<b>x.y.3.n</b>	<b>Method n</b>
<b>x.y.4</b>	<b>Product Subclass 4: Metal–Diene Complexes</b> <i>Synthesis of Product Subclass 4</i>
<b>x.y.4.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 4 in Organic Synthesis</i>
<b>x.y.4.n</b>	<b>Method n</b>
<b>x.y.5</b>	<b>Product Subclass 5: Metal–Allyl Complexes</b> <i>Synthesis of Product Subclass 5</i>
<b>x.y.5.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 5 in Organic Synthesis</i>
<b>x.y.5.n</b>	<b>Method n</b>
<b>x.y.6</b>	<b>Product Subclass 6: Metal–Alkyne Complexes</b> <i>Synthesis of Product Subclass 6</i>
<b>x.y.6.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 6 in Organic Synthesis</i>
<b>x.y.6.n</b>	<b>Method n</b>
<b>x.y.7</b>	<b>Product Subclass 7: Metal–Alkene Complexes</b> <i>Synthesis of Product Subclass 7</i>
<b>x.y.7.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 7 in Organic Synthesis</i>
<b>x.y.7.n</b>	<b>Method n</b>
<b>x.y.8</b>	<b>Product Subclass 8: Metal–Carbene Complexes</b> <i>Synthesis of Product Subclass 8</i>
<b>x.y.8.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 8 in Organic Synthesis</i>
<b>x.y.8.n</b>	<b>Method n</b>
<b>x.y.9</b>	<b>Product Subclass 9: Metal–Carbyne Complexes</b> <i>Synthesis of Product Subclass 9</i>
<b>x.y.9.1</b>	<b>Method 1</b> <i>Applications of Product Subclass 9 in Organic Synthesis</i>
<b>x.y.9.n</b>	<b>Method n</b>
<b>x.y.10</b>	<b>Product Subclass 10: Metal <math>\sigma</math>-Alkyl Homoleptic Complexes</b> <i>Synthesis of Product Subclass 10</i>

x.y.10.1	<b>Method 1</b> <i>Applications of Product Subclass 10 in Organic Synthesis</i>
x.y.10.n	<b>Method n</b>
x.y.11	<b>Product Subclass 11:</b> Metal $\sigma$ -Alkyl Non-Homoleptic Complexes <i>Synthesis of Product Subclass 11</i>
x.y.11.1	<b>Method 1</b> <i>Applications of Product Subclass 11 in Organic Synthesis</i>
x.y.11.n	<b>Method n</b>
x.y.12	<b>Product Subclass 12:</b> Miscellaneous Complexes (i.e., carbonyl complexes, amine complexes, etc.) <i>Synthesis of Product Subclass 12</i>
x.y.12.1	<b>Method 1</b> <i>Applications of Product Subclass 12 in Organic Synthesis</i>
x.y.12.n	<b>Method n</b>

#### **Rule 16 Organization of Methods and Variations within Category 2**

Category 2 includes fully unsaturated heterocycles with no  $sp^3$  carbon or heteroatoms not capable of conjugation, such as  $P\lambda^5$  or  $S\lambda^6$  in a five-membered ring. Compounds with a formal charge, such as pyrylium ion, are included. Compounds that satisfy the  $4n + 2$  rule via tautomeric forms and mesoionic compounds are also included. Systems that cannot be aromatic because of saturated carbon in the ring, such as 1,3-dioxine or oxete, as well as saturated or partially unsaturated heterocycles, are not covered in Category 2. Such systems are integrated into the coverage in Categories 3–5 where appropriate.

**Science of Synthesis** organizes hetarenes in the order of preference:

1. ring size, from smaller to larger,
2. number of heteroatoms, from less to more,
3. kind of heteroatoms in the order of preference: O, S, Se, Te, N, P,
4. valence of like heteroatoms, from higher to lower, such as  $P\lambda^5 > P\lambda^3$  and  $S\lambda^4 > S\lambda^2$ ,
5. annulated hetarenes directly after the corresponding monocyclic hetarene, e.g. oxazole, then benzoxazole,
6. (1) neutral, (2) anionic, (3) radical anion, (4) radical, (5) radical cation, (6) cationic.

Those fused hetarenes that are covered in **Science of Synthesis** as Product Classes or Subclasses are organized according to the ring size of the smallest hetarene component and the number and kind of heteroatoms in that ring, from less to more, as above for monocyclic hetarenes.

When the number and kind of heteroatoms are the same, the order follows the lowest numbers in the name from left to right until a difference is found, i.e. 1,2,3 then 1,2,4 then 1,3,2 then 1,4,2 etc. When trivial names are used, which do not contain numbers in the name, the order follows the lowest numbers for the heteroatoms; e.g. isoxazole (1,2-oxazole) then oxazole (1,3-oxazole).

Coverage should concentrate on the synthesis of the heterocyclic system in question. The main subdivisions for a given Product Class or Subclass are “Synthesis by Ring-Closure Reactions”, “Synthesis by Ring Transformation”, “Aromatization”, and “Synthesis by Substituent Modification”, as shown below. The methods involving ring closure are organized according to the number and kinds of bonds formed; in cases of ambiguity arising from the presence of intermediates, it is at the discretion of the author to decide how many bonds are formed. The methods involving substituent modification are restricted to those relevant to the synthesis of specifically functionalized compounds.

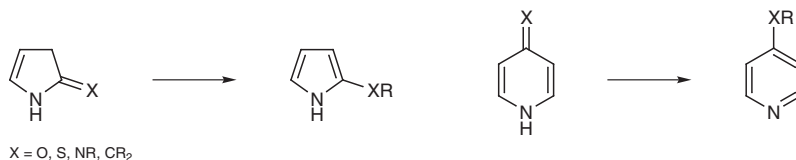
In the coverage of an annulated hetarene, the examples chosen to illustrate a given method could include not only the benzo derivative, but also other areno and hetareno

derivatives to the extent that this inclusion helps to show the scope and limitations of the method.

This leads to the following general arrangement for a **monocyclic hetarene**:

<b>x.y</b>	<b>Product Class Y</b>
	<b>Introductory Text</b>
	Nomenclature, history, applications, reviews (including location in <i>Houben-Weyl</i> ), structure (including tautomerism, ring-chain equilibrium), stability (thermally, towards oxidation/reduction), reactivity (including acidity/basicity, ease of addition and substitution reactions), physical properties, spectroscopic characteristics, safety and environmental aspects
<b>x.y.1</b>	<b>Synthesis by Ring-Closure Reactions</b>
<b>x.y.1.1</b>	By Formation of Three Bonds [Priority: (1) Hetero—Hetero Bond, (2) Hetero—Carbon Bond, (3) Carbon—Carbon Bond; priority of heteroatoms follows Rule 4 and Rule 11]
<b>x.y.1.2</b>	By Formation of Two Hetero—Hetero Bonds (includes cycloadditions; if more than one type of Hetero—Hetero Bond then further ranking according to <b>Science of Synthesis</b> priority rules; further subdivision according to starting material following <b>Science of Synthesis</b> priority rules, e.g. synthesis from CX <sub>4</sub> -, CX <sub>3</sub> -, CX <sub>2</sub> -, CX-hydrocarbon. Reactions involving a final aromatization step are also included here)
<b>x.y.1.3</b>	By Formation of One Heteroatom—Heteroatom and One Heteroatom—Carbon Bond
<b>x.y.1.4</b>	By Formation of Two Heteroatom—Carbon Bonds
<b>x.y.1.5</b>	By Formation of Two C—C Bonds
<b>x.y.1.6</b>	By Formation of One Heteroatom—Heteroatom Bond
<b>x.y.1.7</b>	By Formation of One Heteroatom—Carbon Bond
<b>x.y.1.8</b>	By Formation of One C—C Bond (order of subsections following the nomenclature of the heterocycle, i.e. C1—C2 first, then C2—C3, etc.)
<b>x.y.2</b>	<b>Synthesis by Ring Transformation</b> [ring enlargement, formal exchange of ring members with retention of ring size, ring contraction; ranking of hetarenes according to the priorities given above]
<b>x.y.3</b>	<b>Aromatization (by Oxidation of Dehydro Compounds or Elimination Reactions)</b>
<b>x.y.4</b>	<b>Synthesis by Substituent Modification</b>
<b>x.y.4.1</b>	Substitution of Existing Substituents
<b>x.y.4.1.1</b>	Of Hydrogen [Priority: (1) H/D exchange, (2) metalation, (3) Friedel—Crafts and the like, (4) halogenation, chalcogens, N, P. In tautomeric systems possible loss of the aromatic character.]
<b>x.y.4.1.2</b>	Of Metals [Priority: (1) M → H, (2) transmetalation (cross-reference to Category 1), (3) M → C, (4) M → heteroatom]
<b>x.y.4.1.3</b>	Of Carbon Functionalities (e.g., decarboxylation ... dealkylation, following <b>Science of Synthesis</b> priority rules)
<b>x.y.4.1.4</b>	Of Heteroatoms
<b>x.y.4.2</b>	Addition Reactions (not involving ring modification since this should be included elsewhere, i.e. in the chapter on the ring system which is obtained)
<b>x.y.4.2.1</b>	Protonation
<b>x.y.4.2.2</b>	Addition of Organic Groups (e.g., N-alkylation)
<b>x.y.4.2.3</b>	Addition of Heteroatoms (e.g., N-oxidation)

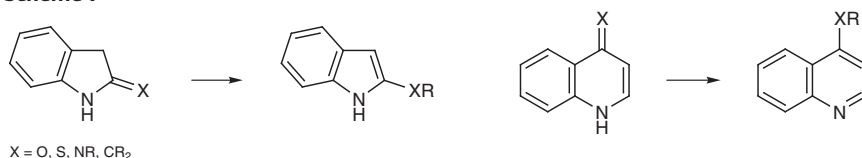
- x.y.4.3** Rearrangement of Substituents  
**x.y.4.4** Modification of Substituents  
 [typically only at the  $\alpha$ -atom since modification at other sites would not be expected to be dependent on the heterocyclic ring system, e.g. oxidation at the  $\alpha$ -carbon; reactions converting an exocyclic double bond into an endocyclic double bond are also included here (Scheme 6), unless they are part of the ring-closure-reaction sequences covered in Section x.y.1]

**Scheme 6**

Similarly, this leads to the following general arrangement for an **annulated hetarene**:

- x.y** **Product Class Y**  
**Introductory Text**  
 Nomenclature, history, applications, reviews (including location in *Houben-Weyl*), structure (including tautomerism, ring-chain equilibrium), stability (thermally, towards oxidation/reduction), reactivity (including acidity/basicity, ease of addition and substitution reactions), physical properties, spectroscopic characteristics, safety and environmental aspects
- x.y.1** **Synthesis by Ring-Closure Reactions**  
**x.y.1.1** By Annulation to an Arene  
**x.y.1.1.1** By Formation of Three Bonds  
 [Priority: (1) Heteroatom–Heteroatom Bond, (2) Heteroatom–Carbon Bond, (3) C–C Bond; priority of heteroatoms follows Rule 4 and Rule 11]  
**x.y.1.1.2** By Formation of Two Heteroatom–Heteroatom Bonds  
 (includes cycloadditions; if more than one type of Hetero–Hetero Bond then further ranking according to **Science of Synthesis** priority rules; further subdivision according to starting material following **Science of Synthesis** priority rules, e.g. synthesis from CX<sub>4</sub><sup>-</sup>, CX<sub>3</sub><sup>-</sup>, CX<sub>2</sub><sup>-</sup>, CX-hydrocarbon. Also reactions involving a final aromatization step are included here)
- x.y.1.1.3** By Formation of One Heteroatom–Heteroatom and One Heteroatom–Carbon Bond  
**x.y.1.1.4** By Formation of Two Heteroatom–Carbon Bonds  
**x.y.1.1.5** By Formation of Two C–C Bonds  
**x.y.1.1.6** By Formation of One Heteroatom–Heteroatom Bond  
**x.y.1.1.7** By Formation of One Heteroatom–Carbon Bond  
**x.y.1.1.8** By Formation of One C–C Bond  
 (order of subsections following nomenclature of the heterocycle, i.e. C1–C2 first, then C2–C3, etc.)
- x.y.1.2** By Annulation to the Heterocyclic Ring  
**x.y.2** **Synthesis by Ring Transformation**  
 [ring enlargement, formal exchange of ring members with retention of the ring size, ring contraction, ranking of hetarenes according to the priorities given above]
- x.y.3** **Aromatization (by Oxidation of Dehydro Compounds or Elimination Reactions)**  
**x.y.4** **Synthesis by Substituent Modification**  
**x.y.4.1** Substitution of Existing Substituents

- x.y.4.1.1** Of Hydrogen  
[Priority: (1) H/D exchange, (2) metalation, (3) Friedel–Crafts and the like, (4) halogenation, chalcogens, N, P. In tautomeric systems possible loss of the aromatic character.]
- x.y.4.1.2** Of Metals  
[Priority: (1) M → H, (2) transmetalation (cross-reference to Category 1), (3) M → C, (4) M → heteroatom]
- x.y.4.1.3** Of Carbon Functionalities  
(e.g., decarboxylation ... dealkylation, following **Science of Synthesis** priority rules)
- x.y.4.1.4** Of Heteroatoms
- x.y.4.2** Addition Reactions  
(not involving ring modification since this should be included elsewhere, i.e. in the chapter on the ring system which is obtained)
- x.y.4.2.1** Protonation
- x.y.4.2.2** Addition of Organic Groups  
(e.g., N-alkylation)
- x.y.4.2.3** Addition of Heteroatoms  
(e.g., N-oxidation)
- x.y.4.3** Rearrangement of Substituents
- x.y.4.4** Modification of Substituents  
[typically only at the  $\alpha$ -atom since modification at other sites would not be expected to be dependent on the heterocyclic ring system, e.g. oxidation at the  $\alpha$ -carbon; reactions converting an exocyclic double bond into an endocyclic double bond are also included here (Scheme 7), unless they are part of the ring-closure-reaction sequences covered in Section x.y.1]

**Scheme 7****Rule 17****Organization of Methods and Variations within Categories 3–6**

Categories 3–6 present the methods for the synthesis of organic compounds organized according to the functional group or groups prepared in the product. The underlying organizational principle is the oxidation state, i.e. all compounds are organized into product classes and product subclasses according to descending oxidation state (see Classification Principles, Section 1.3.1).

Methods and variations within those product classes and subclasses are organized according to Rule 14 (Section 1.3.1.5).

For some compounds, the principal interest to the synthetic chemist is their use as reagents, synthetic building blocks, catalysts, promoters, ligands or auxiliaries. Some reagents may also be highly reactive intermediates, which are not isolated (e.g., some ylides and ketenes). In such cases, synthesis of the product class (or product subclass) and applications of the product class (or product subclass) in organic synthesis should be described. The methods for their application will give products that belong to other product classes within other categories of **Science of Synthesis**, but in the section in question the emphasis will be placed on the role of the product class or product subclass covered.

**Ranking of applied methods** should be carried out:

1. according to the product produced (preferred; see Section 1.3.1.3 and Section 1.3.1.4)
2. according to Rule 14
3. according to the product being discussed  
(e.g., see **Science of Synthesis**, Volume 4, Section 4.4.12:  

4.4.12	Product Subclass 12: Haloorganosilanes...
	Applications of Product Subclass 12 in Organic Synthesis
4.4.12.9	Fluoroorganosilanes
4.4.12.10	Chloroorganosilanes
4.4.12.11	Bromoorganosilanes
4.4.12.12	Iodoorganosilanes)

The **table of contents** should take the following format:

<b>x</b>	<b>Volume x</b>
<b>x.y</b>	<b>Product Class y</b>
<b>x.y.1</b>	<b>Product Subclass 1</b>
<b>x.y.1.1</b>	<b>Synthesis of Product Subclass 1</b>
<b>x.y.1.1.1</b>	<b>Method 1</b>
<b>x.y.1.1.n</b>	<b>Method n</b>
<b>x.y.1.2</b>	<b>Applications of Product Subclass 1 in Organic Synthesis</b>
<b>x.y.1.2.1</b>	<b>Method 1</b>
<b>x.y.1.2.n</b>	<b>Method n</b>
<b>x.y.2</b>	<b>Product Subclass 2</b>
<b>x.y.n</b>	<b>Product Subclass n</b>
<b>x.n</b>	<b>Product Class n</b>

### 1.3.1.6 Examples within Methods and Variations

The scope and limitations of a method or variation should be illustrated with several examples. The accompanying reaction scheme(s) should be made as general as possible by the use of X, R<sup>1</sup>, R<sup>2</sup>, etc. as substituents. If individual examples from a general scheme need to be discussed in the main text, then a table should be employed to present relevant data (e.g., R-groups, reaction conditions, solvents, chromatography conditions, chemical yield, optical purity, etc.) for the examples. If individual examples are not actively referred to in the main text, they should be presented in a scheme table if 8 or more examples are chosen, or they should simply be illustrated within the scheme itself if only a few examples are employed. Full details of the use, construction, and placement within the manuscript of tables, scheme tables, and schemes are given in the **Information for Authors** section.

#### Rule 18 Organization of Examples within Methods and Variations

Irrespective of the mode of presentation (*vide supra*), individual examples used to highlight methods and variations should be listed in an order which the author and/or volume editor believe best illustrates the scope and limitations of each method or variation (e.g., they may be listed in increasing order of substituent/reagent complexity, or in increasing order of chemical or optical yield).

#### Rule 19 Extent of Polymer Coverage

Polymers are considered to be an important class of compounds although they are not traditional target molecules for chemists working in the field of organic synthesis. However,

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a thorough, synthetic and, comprehensive treatment of polymers is beyond the scope of the *Science of Synthesis* series. The focus of *Science of Synthesis* is on the synthesis of important monomeric molecular species. A compromise has been reached by covering the most important methods for polymer synthesis including introductory text together with leading references to more comprehensive reviews, handbooks and the original literature.

## 1.3.2 Complete Volume List of Science of Synthesis

Based on the classification principles outlined in Section 1.3.1, **Science of Synthesis** will be published as the following volumes:

Category and Year	Volume Number	Category Product Class	Number of Volumes	Number of Pages	Responsible Member of the Editorial Board	Volume Editor(s)
<b>1</b>	<b>1–8</b>	<b>Organometallics</b>	<b>8</b>	<b>7052</b>		
2001	1	Compounds with Transition Metal–Carbon $\pi$ -Bonds and Compounds of Groups 10–8 (Ni, Pd, Pt, Co, Rh, Ir, Fe, Ru, Os)		1112	Trost	Lautens
2002	2	Compounds of Groups 7–3 (Mn..., Cr..., V..., Ti..., Sc..., La..., Ac...)		1070	Noyori	Imamoto
2003	3	Compounds of Groups 12 and 11 (Zn, Cd, Hg, Cu, Ag, Au)		846	Ley	O'Neil
2001	4	Compounds of Group 15 (As, Sb, Bi) and Silicon Compounds		1060	Ley	Fleming
2002	5	Compounds of Group 14 (Ge, Sn, Pb)		864	Thomas	Moloney
2004	6	Boron Compounds		840	Regitz/ Schaumann	Kaufmann/ Matteson
2004	7	Compounds of Groups 13 and 2 (Al, Ga, In, Tl, Be ... Ba)		660	Noyori	H. Yamamoto
2004	8	Compounds of Group 1 (Li ... Cs)		600	Trost	Snieckus/ Majewski
<b>2</b>	<b>9–17</b>	<b>Hetarenes and Related Ring Systems</b>	<b>9</b>	<b>9344</b>		
2000	9	Fully Unsaturated Small-Ring Heterocycles and Monocyclic Five-Membered Hetarenes with One Heteroatom		664	Regitz	Maas
2000	10	Fused Five-Membered Hetarenes with One Heteroatom		916	Thomas	Thomas
2001	11	Five-Membered Hetarenes with One Chalcogen and One Additional Heteroatom		1160	Schaumann	Schaumann
2002	12	Five-Membered Hetarenes with Two Nitrogen or Phosphorus Atoms		796	Bellus	Neier
2003	13	Five-Membered Hetarenes with Three or More Heteroatoms		1010	Shinkai	Storr/Gilchrist
2003	14	Six-Membered Hetarenes with One Chalcogen		1010	Thomas	Thomas
2004	15	Six-Membered Hetarenes with One Nitrogen or Phosphorus Atom		720	Regitz	Black
2003	16	Six-Membered Hetarenes with Two Identical Heteroatoms		1568	Shinkai	Y. Yamamoto
2003	17	Six-Membered Hetarenes with Two Unlike or More than Two Heteroatoms and Fully Unsaturated Larger-Ring Heterocycles		1500	Schaumann	Weinreb

Category and Year	Volume Number	Category Product Class	Number of Volumes	Number of Pages	Responsible Member of the Editorial Board	Volume Editor(s)
<b>3</b>	<b>18–24</b>	<b>Compounds with Four and Three Carbon–Heteroatom Bonds</b>	<b>7</b>	<b>5220</b>		
2005	<b>18</b>	Four Carbon–Heteroatom Bonds: X–C≡X, X=C=X, X <sub>2</sub> C=X, CX <sub>4</sub>		1080	Ley	Knight
2004	<b>19</b>	Three Carbon–Heteroatom Bonds: Nitriles, Isocyanides, and Derivatives		480	Shinkai	Murahashi
2005	<b>20</b>	Three Carbon–Heteroatom Bonds: Acid Halides; Carboxylic Acids and Acid Salts; Esters, Polyesters, and Lactones; Peroxy Acids and R(CO)OX Compounds; R(CO)X, X = S, Se, Te		960	Jacobsen	Panek
2005	<b>21</b>	Three Carbon–Heteroatom Bonds: Amides and Derivatives; Polyamides and Peptides; Lactams		720	Shinkai	Weinreb
2005	<b>22</b>	Three Carbon–Heteroatom Bonds: Thio-, Seleno-, and Tellurocarboxylic Acids and Derivatives; Imidic Acids and Derivatives; Ortho Acid Derivatives		540	Thomas	Charette
2005	<b>23</b>	Three Carbon–Heteroatom Bonds: Ketenes and Derivatives		720	Bellus	Danheiser
2005	<b>24</b>	Three Carbon–Heteroatom Bonds: Ketene Acetals and Yne–X Compounds		720	Schaumann	de Meijere
<b>4</b>	<b>25–33</b>	<b>Compounds with Two Carbon–Heteroatom Bonds</b>	<b>9</b>	<b>6180</b>		
2006	<b>25</b>	Aldehydes		480	Schaumann	Brückner
2004	<b>26</b>	Ketones		820	Thomas	Cossy
2004	<b>27</b>	Heteroatom Analogues of Aldehydes and Ketones		680	Bellus	Padwa
2006	<b>28</b>	Quinones and Heteroatom Analogues		600	Bellus	Griesbeck
2006	<b>29</b>	Acetals: Hal/X and O/O, S, Se, Te		840	Ley	Warriner
2006	<b>30</b>	Acetals: O/N, S/S and S/N and Higher Heteroatom Analogues		600	Noyori	Otera
2007	<b>31</b>	Arene–X Compounds		960	Bellus	–
2007	<b>32</b>	X–Ene–X and Ene–O Compounds		720	Schaumann	
2006	<b>33</b>	Ene–X Compounds (X ≠ O)		480	Trost	–

Category and Year	Volume Number	Category Product Class	Number of Volumes	Number of Pages	Responsible Member of the Editorial Board	Volume Editor(s)
<b>5</b>	<b>34–42</b>	<b>Compounds with One Carbon–Heteroatom Bond</b>	<b>9</b>	<b>7560</b>		
2006	<b>34</b>	Fluorine		480	Ley	Percy
2007	<b>35</b>	Chlorine, Bromine, and Iodine		720	Schaumann	–
2007	<b>36</b>	Alcohols		960	Thomas	–
2007	<b>37</b>	Ethers		960	Jacobsen	–
2007	<b>38</b>	Peroxides, Inorganic Esters		840	Shinkai	–
2008	<b>39</b>	Sulfides, Selenides, and Tellurides		1080	Noyori	Kambe
2008	<b>40</b>	Amines, Ammonium Salts, Haloamines, Hydroxylamines, Hydrazines, Triazanes, and Tetrazanes		960	Schaumann	–
2008	<b>41</b>	Nitro, Nitroso, Azo, Azoxy, and Diazonium Compounds, Azides, Triazenes, and Tetrazenes		960	Shinkai	–
2007	<b>42</b>	Organophosphorus Compounds		600	Trost	Vedejs
<b>6</b>	<b>43–48</b>	<b>Compounds with All-Carbon Functions</b>	<b>6</b>	<b>4200</b>		
2008	<b>43</b>	Polyynes, Arynes, Enynes, and Alkynes		720	Thomas	–
2008	<b>44</b>	Cumulenes and Allenes		480	Bellus	–
2007	<b>45</b>	Arenes, Quasiarenes, Annulenes, and Polyenes		840	Shinkai	–
2008	<b>46</b>	1,3-Dienes		600	Trost	
2008	<b>47</b>	Alkenes		960	Jacobsen	–
2008	<b>48</b>	Alkanes		600	Schaumann	–

**Science of Synthesis** will be published in a total number of 48 volumes, which will contain approximately 35 000 pages. It is estimated that **Science of Synthesis** will contain 5000 methods, 10 000 variations, 15 000 reaction schemes, and 15 000 tables. **Science of Synthesis** will cover ca. 150 000 reactions.