Science of Synthesis

Knowledge Updates 2018/3

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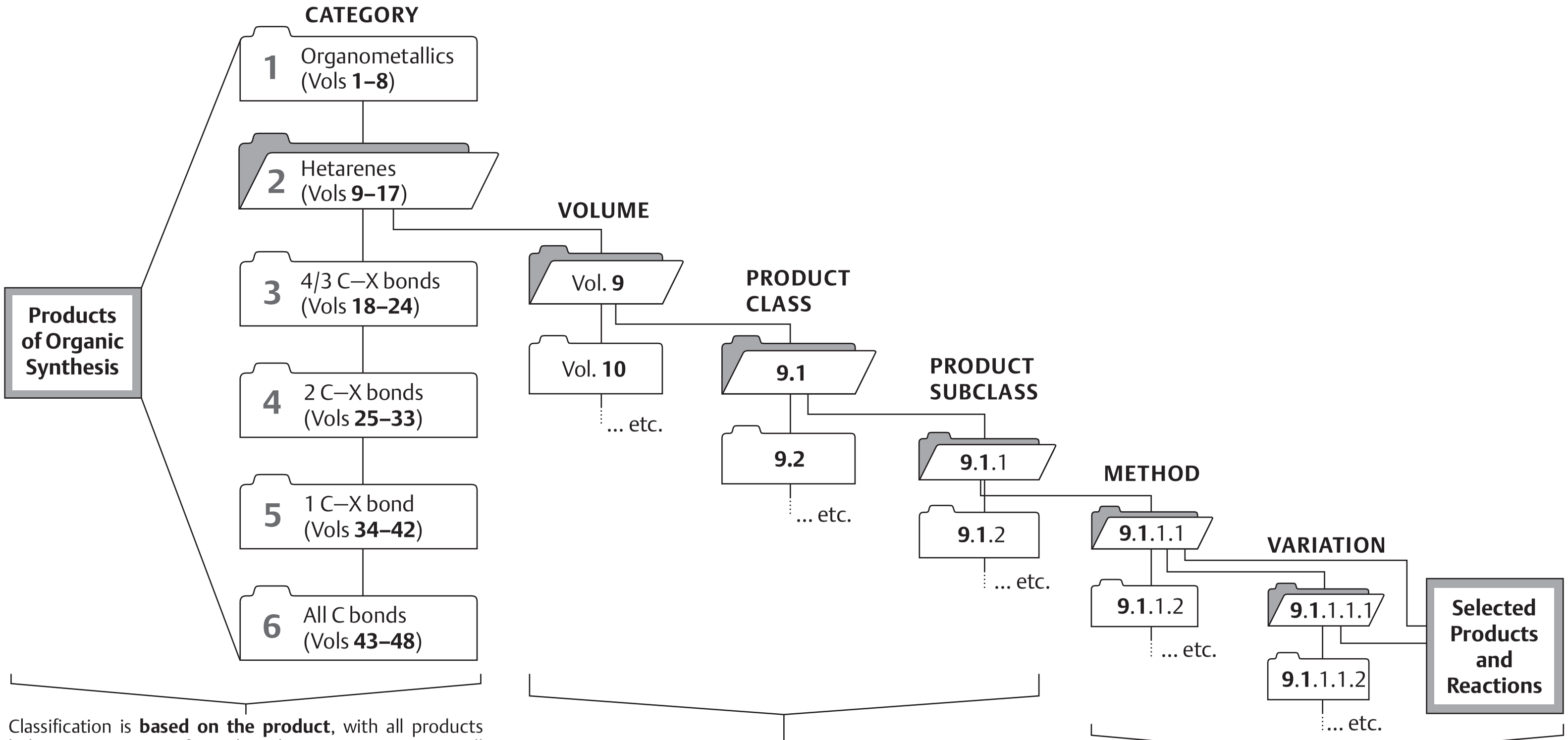

Classification is **based on the product**, with all products belonging to one of six broad-ranging categories. All products occupy a strict hierarchical position in Science of Synthesis, defined according to the classification principles*. Products in Categories 3–6 are organized according to oxidation state, with products containing the greatest number of carbon–heteroatom (C—X) or C—C π-bonds to a single carbon occupying the highest positions (e.g., carboxylates, enolates, and alcoholates are covered in Categories 3, 4, and 5, respectively).

Each category is subdivided into volumes (see opposing page), each of which is devoted to discrete groupings of compounds called **product classes** (e.g., “Thiophenes” is Product Class 10 of Volume 9). Product classes may be further subdivided into **product subclasses**, (e.g., “Thiophene 1,1-Dioxides” is Product Subclass 3 of Product Class 10 of Volume 9). Consequently, the relationship between heading name and heading number varies below product class level within individual volumes.

For each product class or subclass, a number of methods are described for synthesizing the general product type. Often there are variations on a method given. Both methods and variations contain experimental procedures with relevant background information and literature references. **Selected products and reactions** display the scope and limitations of the methods.

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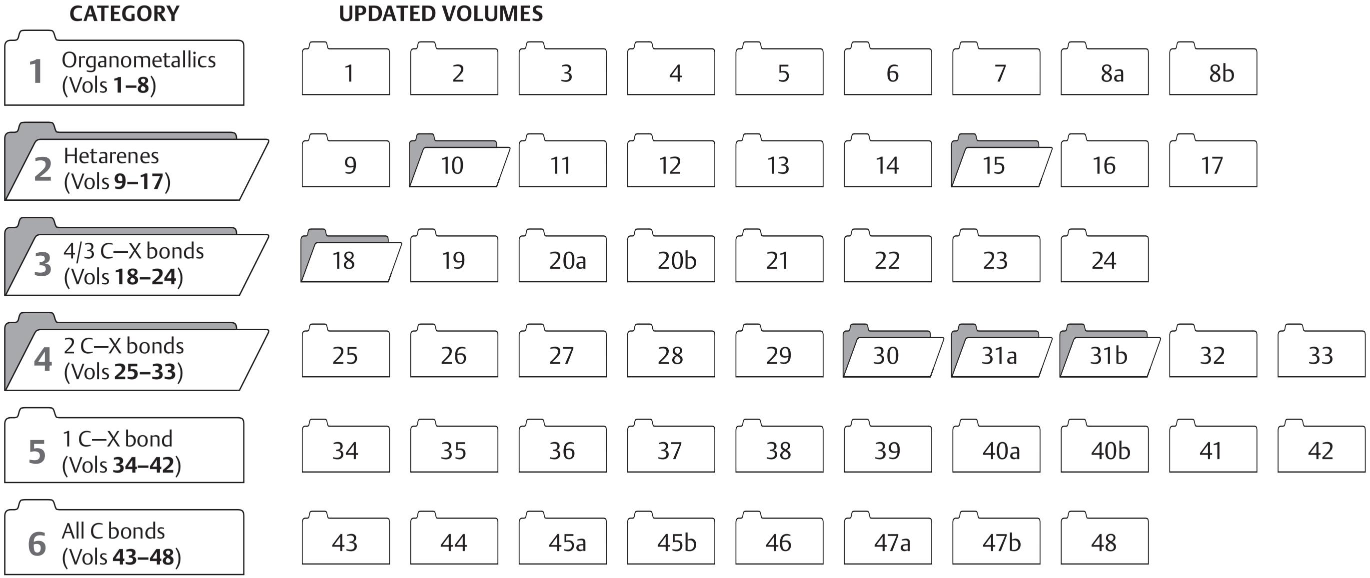
* A complete description of the full classification principles can be found in the **Science of Synthesis Guidebook.**



CATEGORY	UPDATED VOLUMES									
1 Organometallics (Vols **1–8**)	1	2	3	4	5	6	7	8a	8b	
2 Hetarenes (Vols **9–17**)	9	10	11	12	13	14	15	16	17	
3 4/3 C—X bonds (Vols **18–24**)	18	19	20a	20b	21	22	23	24		
4 2 C—X bonds (Vols **25–33**)	25	26	27	28	29	30	31a	31b	32	33
5 1 C—X bond (Vols **34–42**)	34	35	36	37	38	39	40a	40b	41	42
6 All C bonds (Vols **43–48**)	43	44	45a	45b	46	47a	47b	48		

10 Fused Five-Membered Hetarenes with One Heteroatom
15 Six-Membered Hetarenes with One Nitrogen or Phosphorus Atom
18 Four Carbon—Heteroatom Bonds: X—C≡X, X=C=X, X_2C=X, CX_4
30 Acetals: O/N, S/S, S/N, and N/N and Higher Heteroatom Analogues
31a Arene—X (X = Hal, O, S, Se, Te)
31b Arene—X (X = N, P)

* Detailed listings of product classes and subclasses, methods, and variations can be found in the **Table of Contents** sections of every volume.

Science of Synthesis

Science of Synthesis is the authoritative and comprehensive reference work for the entire field of organic and organometallic synthesis.

Science of Synthesis presents the important synthetic methods for all classes of compounds and includes:

- Methods critically evaluated by leading scientists
- Background information and detailed experimental procedures
- Schemes and tables which illustrate the reaction scope

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Preface

As the pace and breadth of research intensifies, organic synthesis is playing an increasingly central role in the discovery process within all imaginable areas of science: from pharmaceuticals, agrochemicals, and materials science to areas of biology and physics, the most impactful investigations are becoming more and more molecular. As an enabling science, synthetic organic chemistry is uniquely poised to provide access to compounds with exciting and valuable new properties. Organic molecules of extreme complexity can, given expert knowledge, be prepared with exquisite efficiency and selectivity, allowing virtually any phenomenon to be probed at levels never before imagined. With ready access to materials of remarkable structural diversity, critical studies can be conducted that reveal the intimate workings of chemical, biological, or physical processes with stunning detail.

The sheer variety of chemical structural space required for these investigations and the design elements necessary to assemble molecular targets of increasing intricacy place extraordinary demands on the individual synthetic methods used. They must be robust and provide reliably high yields on both small and large scales, have broad applicability, and exhibit high selectivity. Increasingly, synthetic approaches to organic molecules must take into account environmental sustainability. Thus, atom economy and the overall environmental impact of the transformations are taking on increased importance.

The need to provide a dependable source of information on evaluated synthetic methods in organic chemistry embracing these characteristics was first acknowledged over 100 years ago, when the highly regarded reference source **Houben–Weyl Methoden der Organischen Chemie** was first introduced. Recognizing the necessity to provide a modernized, comprehensive, and critical assessment of synthetic organic chemistry, in 2000 Thieme launched **Science of Synthesis, Houben–Weyl Methods of Molecular Transformations**. This effort, assembled by almost 1000 leading experts from both industry and academia, provides a balanced and critical analysis of the entire literature from the early 1800s until the year of publication. The accompanying online version of **Science of Synthesis** provides text, structure, substructure, and reaction searching capabilities by a powerful, yet easy-to-use, intuitive interface.

From 2010 onward, **Science of Synthesis** is being updated quarterly with high-quality content via **Science of Synthesis Knowledge Updates**. The goal of the **Science of Synthesis Knowledge Updates** is to provide a continuous review of the field of synthetic organic chemistry, with an eye toward evaluating and analyzing significant new developments in synthetic methods. A list of stringent criteria for inclusion of each synthetic transformation ensures that only the best and most reliable synthetic methods are incorporated. These efforts guarantee that **Science of Synthesis** will continue to be the most up-to-date electronic database available for the documentation of validated synthetic methods.

Also from 2010, **Science of Synthesis** includes the **Science of Synthesis Reference Library**, comprising volumes covering special topics of organic chemistry in a modular fashion, with six main classifications: (1) Classical, (2) Advances, (3) Transformations, (4) Applications, (5) Structures, and (6) Techniques. Titles will include *Stereoselective Synthesis*, *Water in Organic Synthesis*, and *Asymmetric Organocatalysis*, among others. With expert-evaluated content focusing on subjects of particular current interest, the **Science of Synthesis Reference Library** complements the **Science of Synthesis Knowledge Updates**, to make **Science of Synthesis** the complete information source for the modern synthetic chemist.

The overarching goal of the **Science of Synthesis** Editorial Board is to make the suite of **Science of Synthesis** resources the first and foremost focal point for critically evaluated information on chemical transformations for those individuals involved in the design and construction of organic molecules.

Throughout the years, the chemical community has benefited tremendously from the outstanding contribution of hundreds of highly dedicated expert authors who have devoted their energies and intellectual capital to these projects. We thank all of these individuals for the heroic efforts they have made throughout the entire publication process to make **Science of Synthesis** a reference work of the highest integrity and quality.

The Editorial Board July 2010

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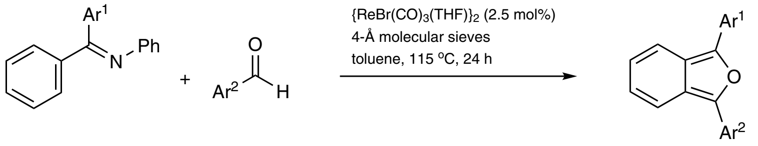
Abstracts

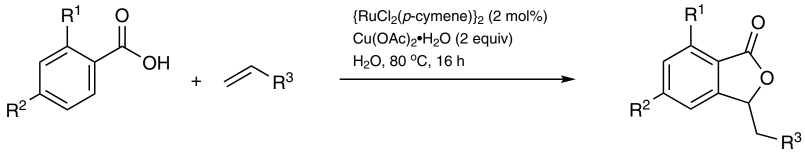
2018 p 1

10.2 Product Class 2: Benzo[*c*]furan and Its Derivatives

H. Kwiecień

This chapter is a revision of the earlier *Science of Synthesis* contribution describing methods for the synthesis of benzo[*c*]furans (isobenzofurans), and has been expanded to include 1,3-dihydrobenzo[*c*]furan-1(3*H*)-ones [1,3-dihydroisobenzofuran-1(3*H*)-ones, phthalides]. Various methods for the in situ generation of the very reactive benzo[*c*]furans and their trapping with dienophiles through Diels–Alder reactions, as well as approaches to the preparation of stable 1,3-diarylbenzo[*c*]furans, are presented. Classical routes to 1,3-dihydrobenzo[*c*]furan-1(3*H*)-ones involve the disproportionation of 1,2-diacylbenzenes or formation of the lactone ring from 2-functionalized benzoic acid derivatives. More recent developments that involve other approaches are also included.





R^3 = CN, CO_2Me

Keywords: benzo[*c*]furans · isobenzofurans · 1,3-dihydrobenzo[*c*]furan-1(3*H*)-ones · phthalides · organometallic reagents · transition-metal catalysts · cyclization · Diels–Alder cycloaddition · retro-Diels–Alder reaction · lactonization · pyrolysis · asymmetric reaction · ring transformation · aromatization

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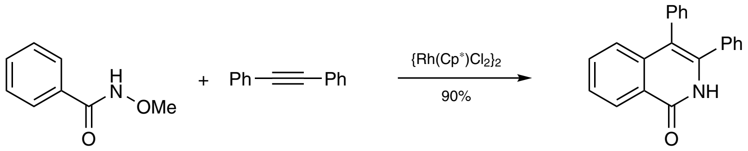
15.6.3 Isoquinolinones

V. A. Glushkov and Yu. V. Shklyaev

This chapter is an update to the earlier *Science of Synthesis* contribution describing methods for the synthesis of isoquinolin-1(2*H*)-ones and isoquinolin-3(2*H*)-ones. The focus is on the literature published in the period 2005–2015, and includes new cyclization reactions, C—H activation methods, and catalysis by metal complexes of nickel, ruthenium, rhodium, and palladium.



Keywords: isoquinolines · isoquinolinones · benzamides · cyclization · lactamization · C—H bond activation · annulation · acetylenes · transition-metal catalysis · nickel · ruthenium · rhodium · palladium

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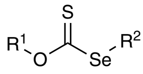
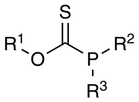
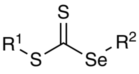
18.10.15 Thiocarbonic Acids and Derivatives

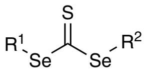
R. A. Aitken

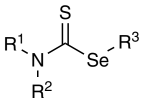
This chapter is an update to the earlier *Science of Synthesis* contribution (Section 18.10) describing methods for the synthesis of thiocarbonic acids and derivatives and their applications in organic synthesis. In addition to new methods and applications for the more common derivatives covered in the original chapter, synthesis and applications of several less common systems are included for the first time.

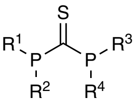












Keywords: sulfur compounds · selenium compounds · tellurium compounds · thiocarbonyl compounds · thiocarbamates · thionyl compounds · thioureas · dithiocarbonates · dithiocarbamates

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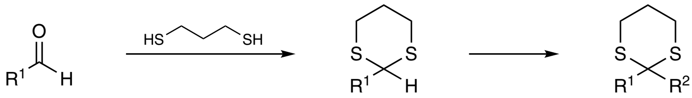
30.3.4.3 1,3-Dithianes

Y. Saikawa and M. Nakata

1,3-Dithianes are widely used as carbonyl protecting groups as they are stable under both acidic and basic conditions. They are intermediates in desulfurization reactions and they also enable carbonyl umpolung by metalation. This chapter discusses advances in 1,3-dithiane synthesis published since 2007, including solid-supported thioacetalization reactions.



Keywords: acetalization · umpolung · dithianes · metalation · dithiols

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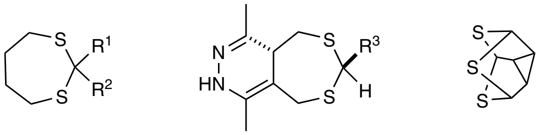
30.3.5.3 1,3-Dithiepanes

Y. Saikawa and M. Nakata

1,3-Dithiepanes are less common than 1,3-dithiolanes or 1,3-dithianes, but are also used in the thioacetalization of carbonyl compounds. This chapter covers methods published since 2007, including fused rings with hidden 1,3-dithiepane substructures.



Keywords: dithiepanes · Lewis acid catalyzed reactions · acetalization · fused-ring systems · dithiols

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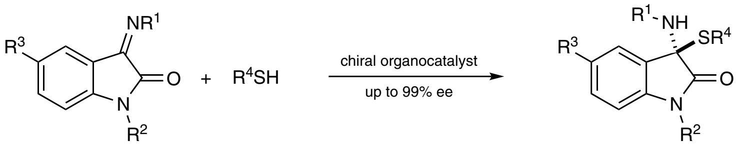
30.4.3 *S,N*-Acetals (α-Amino Sulfur Derivatives)

Y. Mutoh

This chapter is an update to the earlier *Science of Synthesis* contribution (Section 30.4) describing methods for the synthesis of *S*,*N*-acetals (also known as *N*,*S*-acetals or α-amino sulfur derivatives) that have been reported since 2003. One of the major recent developments involves the enantioselective synthesis of *S*,*N*-acetals by organocatalysis.



Keywords: *S*,*N*-acetals · α-amino sulfur derivatives · alkynylation · nucleophilic addition · phase-transfer catalysis · asymmetric catalysis · acid catalysts · electrophilic additions · cycloadditions · sulfur compounds · thiols · iminium salts

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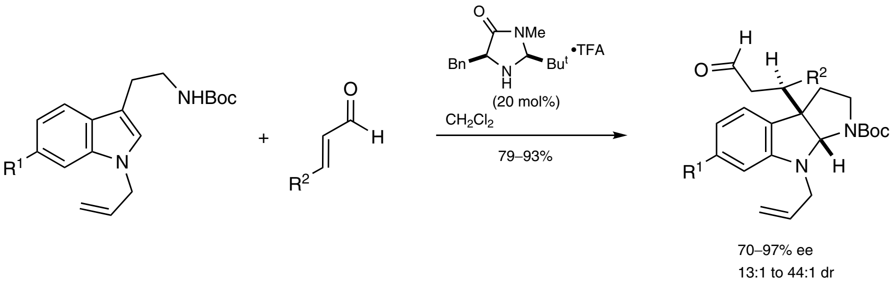
30.6.3 *N,N*-Acetals (Aminals)

Y. Mutoh

This chapter is an update to the earlier *Science of Synthesis* contribution (Section 30.6) describing methods for the synthesis of *N*,*N*-acetals (also known as aminals) that have been reported since 2003. The major recent advances include methods for the enantioselective synthesis of *N*,*N*-acetals by organocatalysis and by transition-metal catalysis.



R^1 = H, Br; R^2 = H, Bz, CO$_2$Me

Keywords: *N*,*N*-acetals · aminals · alkylation · nucleophilic addition · asymmetric catalysis · acid catalysts · electrophilic additions · cycloadditions · hetero-Diels–Alder reactions · imines · palladium catalysts · iridium catalysts

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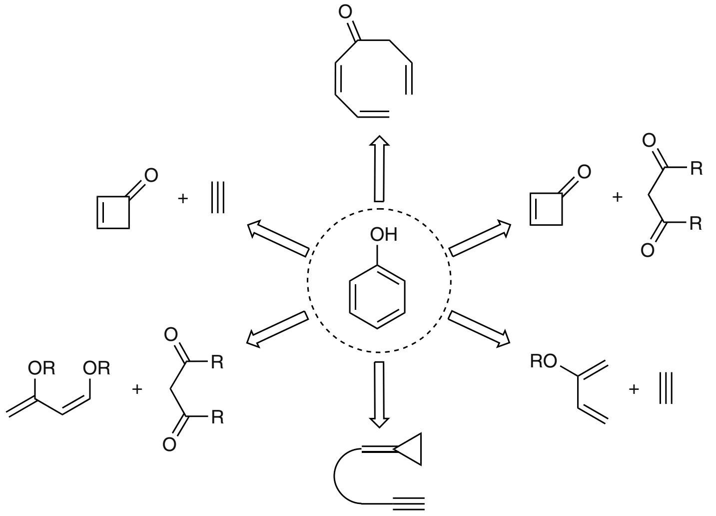
31.5.1.5.12 Synthesis of Phenols from Nonaromatic Precursors

C. González-Bello

The introduction, or chemical modification, of substituents on an existing aromatic ring is probably the most widely employed strategy for the synthesis of phenols, and these methods are summarized in Sections 31.5.1.1 to 31.5.1.4. However, with such transformations, it is sometimes difficult to achieve satisfactory regiocontrol. Furthermore, the required precursors may be expensive, difficult to synthesize, or simply unavailable. The direct construction of a phenol ring from acyclic precursors that already bear the required substituents at the appropriate positions represents a good alternative. This strategy is particularly useful for the synthesis of highly substituted phenols. In this chapter, an update of the reported methods for this approach, which were originally described in Section 31.5.1.5 of *Science of Synthesis* in 2007, is provided, and includes methods for benzannulation, cycloaromatization, cyclocondensation, and ring-closing metathesis.



Keywords: phenols · benzannulation · cycloaromatization · cyclizations · cyclocondensation · ring-closing metathesis · Diels–Alder reactions

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Volume 15: Six-Membered Hetarenes with One Nitrogen or Phosphorus Atom

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15.6 Product Class 6: Isoquinolinones

15.6.3 **Isoquinolinones** 2018

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18.10 Product Class 10: Thiocarbonic Acids and Derivatives

18.10.15 Thiocarbonic Acids and Derivatives (2018)

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