

Abstracts

New

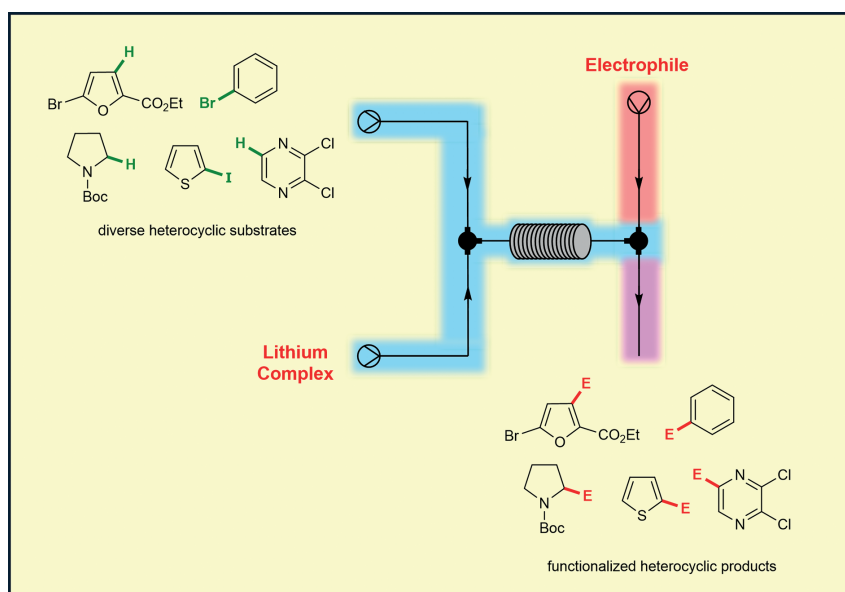
8.1.38

Lithiation of Heterocycles in Continuous Flow

Graeme Barker

p 1

Heterocycles underpin almost all aspects of modern life, occurring in almost all pharmaceuticals and playing key roles in agrochemicals, materials, and catalysts. The use of continuous flow chemistry in small molecule synthesis, including heterocyclic synthesis is well understood and offers fundamental advantages in terms of mass- and heat-transfer, efficiency and process safety. Lithiation of heterocycles is similarly well understood, with access to lithiated heterocycles via a variety of methods including deprotolithiation, carbolithiation, and lithium–halogen exchange. Subsequent uses of lithiated heterocycles are similarly diverse, and include electrophilic trapping, transmetalations to other organometallic species, and addition to arynes, alkynes and alkenes. In this review, a comprehensive overview of heterocycle lithiation in continuous flow is presented, including aromatic and saturated N-, O- and S-heterocycle substrates.



Keywords: heterocycles · lithiation · continuous flow · deprotolithiation · carbolithiation · halogen–lithium exchange

2026

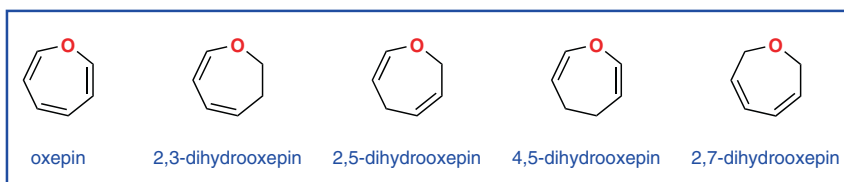
p 139

17.4.1.6

Oxepins

Shaohui Yu and Xi Wang

This review provides an update on oxepin synthesis, with a focus on methodologies developed since 2012. Furthermore, comprehensive coverage of dihydrooxepin synthesis is included, reflecting the significant growth of synthetic methods for these derivatives. Both oxepin and dihydrooxepin moieties are present in various natural products and exhibit diverse biological activities. However, the synthesis of these medium-sized oxygen heterocycles remains challenging due to high ring strain, and instability arising from isomerization. The synthetic strategies discussed herein include cyclization, cycloaddition, pericyclic rearrangements, and ring-expansion reactions.



Keywords: oxepins · dihydrooxepins · Baeyer–Villiger oxidation · retro-Claisen rearrangement · Cope rearrangement · cycloaddition · annulation · ring expansion · cyclization

2026

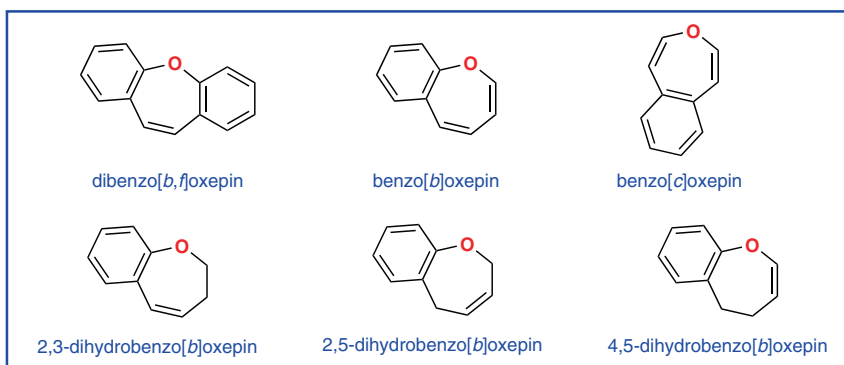
p 161

17.4.2.6

Benzoxepins

Shaohui Yu and Xi Wang

This review covers methods for the synthesis of benzoxepins, and represents a further update to previous *Science of Synthesis* contributions on this topic (published in 2004 and 2012). Dihydrobenzoxepin are included, reflecting the emergence of a growing number of synthetic methods for these ring systems. Significant pharmacological activities of these derivatives are highlighted. These include antiproliferative, anti-inflammatory, and antioxidant effects observed in natural products such as pacharin and bauhinoxepin A. Diverse approaches for the synthesis of these seven-membered oxygen heterocycles are covered, including cycloadditions and ring-closure or ring-enlargement transformations. Recent advances in catalytic approaches are also highlighted.



2026

Updated Section ·

2026

Completely Revised Contributions ·

New

New Contributions

Keywords: benzoxepins · dihydrobenzoxepins · annulation · ring-closing metathesis · ring expansion · Overmann rearrangement · Friedel–Crafts reaction · Knoevenagel condensation · Ullmann coupling · Catellani reaction · Mizoroki–Heck reaction · regioselectivity · stereoselectivity

2026

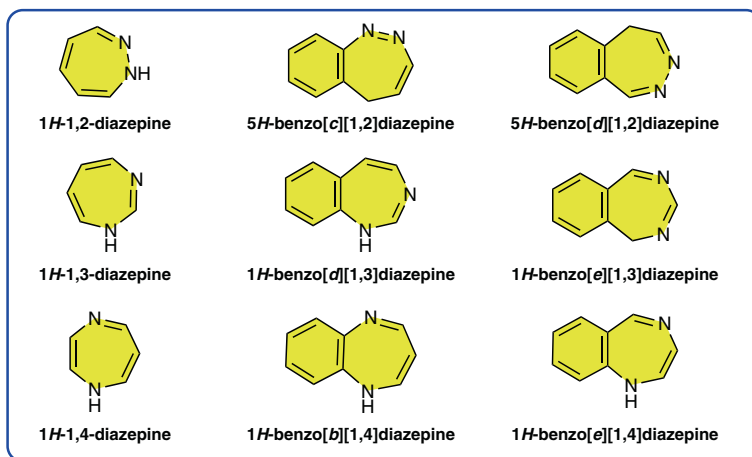
p 209

17.5.5

Diazepines and Benzodiazepines

Daoqian Chen

This update covers synthetic methods for the preparation of seven-membered hetarenes with two or more heteroatoms (N, O, S) that were published between 2013 and 2024, mainly focusing on ring systems with two nitrogen atoms. Diazepine frameworks represent important structural motifs in natural products, pharmaceuticals, and functional materials, as evidenced by approved drugs, bioactive natural products, and emerging materials applications. This review highlights representative 1,2-, 1,3-, and 1,4-diazepines and outlines the principal synthetic approaches to these scaffolds.



Keywords: diazepines · benzodiazepines · cyclization · condensation · ring enlargement · heterocycles · 1,2-diamines · Ugi reaction

2026

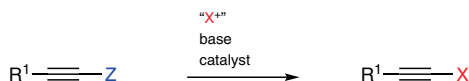
p 297

24.4.1.4 1-Haloalk-1-ynes and Alk-1-yn-1-ols

Mogens Brøndsted Nielsen

This review is an update to the earlier *Science of Synthesis* contributions (Section 24.4.1 and Section 24.4.1.3 from 2006 and 2014, respectively) describing methods for the synthesis of 1-haloalk-1-ynes. It focuses on the literature published since the last update in 2014 up until the last quarter of 2025.

Recent advances in halogenation strategies are highlighted, including numerous mild and selective protocols employing N-haloimides and silver-based catalysts. The review also summarizes expanded applications of haloalkynes in metal-catalyzed transformations, particularly new gold-catalyzed cycloadditions and C–H functionalizations, showing the versatility of these reactive intermediates in synthesis.



Z = H, SiR²₃, CO₂H; X = F, Cl, Br, I

Keywords: alkynes · metal-catalyzed couplings · dehydrohalogenation · halogenation · succinimides

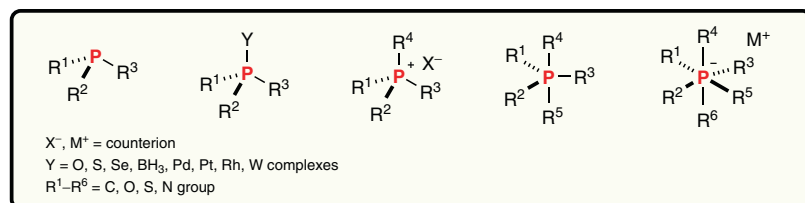
New

p 315

42.20 Development of P-Stereogenic Phosphorus Compounds

Jérôme Bayardon, Raluca Malacea-Kabbara, and Sylvain Jugé

P-Stereogenic phosphorus compounds are of significant current interest in natural products, agrochemistry, pharmaceuticals, materials science, catalysis, and as chemical reagents. Depending on their structure, the chirality of phosphorus compounds may arise from the carbon framework, from the phosphorus center itself (P-chirogenic), or from a combination of both. In recent years, P-chirogenic phosphoramidate and phosphorothioate derivatives of oligonucleotides have attracted considerable attention as DNA analogues, either for binding the complementary regions of messenger RNA in cell nuclei or for enhancing nuclease resistance. As a result, several antiviral and antisense drugs, used in the treatment of hypercholesterolemia, Duchenne muscular dystrophy, and spinal muscular atrophy, have now received approval from international regulatory agencies. Given the increasing importance of phosphorus chirality, particularly in asymmetric catalysis and DNA-based therapeutics, this review provides an overview of the preparation of all classes of P-stereogenic tri- to hexacoordinate compounds, with particular emphasis on systems in which chirality resides at the phosphorus atom. Enantiomerically pure P-stereogenic compounds can be obtained via resolution of racemates, deracemization, stereoselective synthesis employing chiral auxiliaries (such as menthol, amino alcohols, BINOLs, sparteine, amines, diamines, hydroxy thiols, and aminophenols), or through asymmetric catalytic processes.



2026

Updated Section ·

2026

Completely Revised Contributions ·

New

New Contributions

Keywords: P-stereogenic · P-chirogenic · P-chirotopic · phosphinites · phosphonites · phosphites · phosphines · phosphinates · phosphonates · phosphates · phosphine-boranes · phosphine sulfides · phosphine oxides · phosphinothioic acid · phosphonothioates · phosphorothioates · phosphoramidates · phosphonium salts · phosphoranes · hexacoordinated phosphates