

Table of contents

Recent advances in the synthesis of quinoxalin-2(1H)-one derivatives through direct C3-H functionalization **1***Xiang-Kui He, Juan Lu, Lei Li, Jun Xuan*

1. Introduction
2. C3–H Functionalization of quinoxalin-2(1H)-ones
 - 2.1. C3–H Alkylation
 - 2.2. C3–H Arylation
 - 2.3. C3–H Acylation
 - 2.4. C3–H Cyanation
 - 2.5. C3–H Alkoxylation and sulfonylation
 - 2.6. C3–H Amination and amidation
 - 2.7. C3–H Phosphonation
3. Conclusion
- Acknowledgement
- References

Enantioselective synthesis of unsaturated γ -lactams **22***Xabier del Corte, Aitor Maestro, Edorta Martinez de Marigorta, Francisco Palacios, Javier Vicario*

1. Introduction
2. Enantioselective synthesis of 1,5-dihydropyrrol-2-ones
 - 2.1. Vinylogous Michael reactions
 - 2.1.1. Conjugate addition to α,β -unsaturated α,β -unsaturated aldehydes
 - 2.1.2. Conjugate addition to α,β -unsaturated ketones
 - 2.1.3. Conjugate addition to nitroolefins
 - 2.1.4. Vinylogous Michael 1,6-additions
 - 2.2. Vinylogous Mukaiyama reactions
 - 2.3. Dearomatization and desymmetrization reactions
 - 2.4. Mannich reactions
 - 2.5. Other methodologies
3. Enantioselective synthesis of 1,3-dihydropyrrol-2-ones
4. Conclusion
- Acknowledgement
- References

Synthesis of chiral heterocycles through enantioselective metal-catalyzed domino reactions **53***Hélène Pellissier*

1. Introduction
2. Synthesis of monocyclic heterocycles
 - 2.1. Pyrrolidines
 - 2.2. Other monocyclic heterocycles
3. Synthesis of bicyclic heterocycles
 - 3.1. Oxygenated heterocycles
 - 3.2. Nitrogenated heterocycles
4. Synthesis of tricyclic heterocycles
5. Synthesis of tetracyclic heterocycles
6. Conclusion
- References

Application of vinylsulfonium salts to the synthesis of heterocycles

78

Vincent K. Duong, Eoghan M. McGarrigle

1. Introduction
2. Synthesis of vinylsulfonium salts
 - 2.1 Synthesis of α -substituted vinylsulfonium salts
 - 2.2 Synthesis of β -substituted vinylsulfonium salts
 - 2.3 Synthesis of chiral vinylsulfonium salts
3. Synthesis of non-fused 3-membered heterocycles
4. Synthesis of 4-membered heterocycles
5. Synthesis of non-fused 5-membered heterocycles
6. Synthesis of non-fused 6-membered heterocycles
7. Synthesis of non-fused 7-membered heterocycles
8. Synthesis of fused bicyclic heterocyclic ring systems
9. Conclusions
- Acknowledgements
- References

C3-Indazole functionalization: a review

100

Francis Giraud, Fabrice Anizon, Pascale Moreau

1. Introduction
2. Halogenation
 - 2.1. Iodination
 - 2.2. Bromination
 - 2.3. Chlorination
3. Alkylation
4. Alkenylation
5. (Hetero)arylation
6. Acylation
7. Formylation
8. Nitration
9. Amination
10. Borylation
11. Sulfenylation
12. Sulfonylation
13. Selenylation
14. Conclusion
- References

Synthetic approaches to spiro bis-THF natural products: cephalosporolides, penisporolides, ascospiroketals and pyrenolides

113

Rodney A. Fernandes, Ashvin J. Gangani, Naveen Chandra

1. Introduction
2. Total syntheses of cephalosporolides E and F
3. Total synthesis of cephalosporolides H, I and penisporolides A and B
4. Total synthesis of ascospiroketals A and B
5. Total synthesis of pyrenolide D
6. Conclusion
- Acknowledgement
- References

Cobalt-catalyzed picolinamide-directed synthesis of heterocycles

144

Lukass Lukasevics, Liene Grigorjeva

1. Introduction
 2. C-H functionalization with alkynes
 3. C-H functionalization with CO or CO surrogates
 4. C-H functionalization with heteroarenes
 5. Conclusions
- Acknowledgement
References

Synthesis, reactivity and biological properties of methoxy-activated indoles

162

Ibrahim F. Sengul, Murat Bingul, Hakan Kandemir, Naresh Kumar, David StC. Black

1. Introduction
 2. The indole nucleus and its chemistry
 3. Synthesis of methoxy-activated indoles
 4. Methoxy activated bis-indoles and bis-indolyl synthesis
 5. Functionalization of activated indoles
 - 5.1. Halogenation
 - 5.2. Dakin oxidation
 - 5.3. Cyclisation
 6. Indole fused-ring systems
 7. Biological activities of indole analogs
 - 7.1. Anticancer activity
 - 7.2. Anti-HIV activity
 - 7.3. Antibacterial activity
 - 7.4. Anticholinesterase activity
 - 7.5. Antidepressant activity
 - 7.6. Antihistaminic activity
 - 7.7. Anti-inflammatory activity
 - 7.8. Antimalarial activity
 - 7.9. Anti-Parkinson activity
 - 7.10. Antimicrobial activity
 - 7.11. Antioxidant activity
 - 7.12. Antitumor activity
 - 7.13. Receptor inhibitors
 - 7.14. Tubulin inhibitors
 8. Indole natural products
 9. Conclusions
- Acknowledgements
References

Epoxides as dual-functionalized alkylating reagents for the assembly of oxygen-containing heterocycles

213

Ze-Shui Liu, Hong-Gang Cheng, Qianghui Zhou

1. Introduction
2. Assembly of six-membered oxygen-containing heterocycles
 - 2.1. Synthesis of 3,4-dihydroisocoumarins
 - 2.2. Synthesis of isochromans
 - 2.3. Synthesis of dihydropyran derivatives
 - 2.4. Synthesis of morpholine derivatives
3. Assembly of five-membered oxygen-containing heterocycles
 - 3.1. Synthesis of 2,3-dihydrobenzofuran

- 3.2. Synthesis of isobenzofuranone
- 4. Conclusion
- Acknowledgements
- References

1,6-Addition-based annulation reactions for the synthesis of oxa- and aza-heterocycles 229

Bo Jiang, Jia-Yin Wang

- 1. Introduction
- 2. Synthesis of O-containing heterocycles
- 3. Synthesis of N-containing heterocycles
- 4. Synthesis of O and N-containing heterocycles
- 5. Conclusion
- Acknowledgement
- References

Biomimetic cascade strategies towards 2-aminoindolines from alkaloids 256

Timo van Schaik, Jordy M. Saya, Eelco Ruijter, Romano V. A. Orru

- 1. Introduction
- 2. Synthesis of pyrroloindolines
 - 2.1. Electrophilic addition
 - 2.2. Addition to π -allyl complex
 - 2.3. Michael type reaction
 - 2.4. 1,3-Dipolar cycloaddition
 - 2.5. Radical cyclization
 - 2.6. Interrupted Pummerer reaction
 - 2.7. Carbene insertion
 - 2.8. Fischer type indolization
- 3. Synthesis of pyridinoindolines
 - 3.1. Diels-Alder type reaction
 - 3.2. Copper catalyzed cascade reaction
- 4. Synthesis of 2,3-fused pyrroloindolines
 - 4.1. Diels-Alder type reaction
 - 4.2. Nucleophilic aromatic substitution
- 5. Synthesis of 3,3-spiropyrrroloindolines
 - 5.1. Gold alkyne catalysis
 - 5.2. Oxidative coupling
 - 5.3. Interrupted Ugi type reaction
 - 5.4. Fischer type indolization
- 6. Conclusion and outlook
- References

Assessment of the impact of continuous flow chemistry on modern heterocyclic chemistry 281

Cormac Bracken, Marcus Baumann

- 1. Introduction to flow chemistry
- 2. Flow chemistry and its applications in heterocycle synthesis
 - 2.1. De novo synthesis of heterocyclic targets
 - 2.2. Heterocycle transposition reactions
 - 2.3. Heterocycle functionalisation processes
- 3. Conclusion
- Acknowledgement
- References

State-of-the-art approaches to the synthesis of 2H-pyrroles**308***Artem Petrenko, Sergej Mrkobrađa, Tomáš Tobrman*

1. Introduction
 2. Synthesis of 2H-pyrroles by means of transition-metal-catalyzed reactions
 - 2.1. Iridium-, rhodium-, and silver-catalyzed synthesis of 2H-pyrroles
 - 2.2. Palladium-catalyzed synthesis of 2H-pyrroles
 3. Transition-metal-free synthesis of 2H-pyrroles
 4. Synthesis of 3H-pyrroles
 5. Conclusion
- Acknowledgements
References

Synthesis of functionalized furan derivatives by generation of 2-(furyl)carbene intermediates**326***Olaya Bernado, Luis A. López*

1. Introduction
 2. Metal-free approaches
 3. Transition-metal-catalyzed transformations involving (2-furyl)carbene intermediates
 - 3.1. Copper-catalyzed synthesis of functionalized furans via (2-furylcarbene) complexes
 - 3.2. Zinc-catalyzed synthesis of functionalized furans via (2-furylcarbene) complexes
 4. Conclusions
- Acknowledgement
References

Synthesis of modified tryptophan derivatives**342***Lukas Junk, Angelika Ullrich, Uli Kasmaier*

1. Introduction
 2. Coupling of indoles to the amino acid backbone via C–C bond formation
 - 2.1. Alkylation of chiral auxiliaries
 - 2.2. Asymmetric hydrogenation of dehydroamino acids
 - 2.3. Negishi coupling
 - 2.4. Aziridine opening
 - 2.5. Friedel-Crafts conjugate addition to 2-aminoacrylates
 - 2.6. β -C(sp³)–H activation of alanine derivatives
 - 2.7. Enzymatic approaches
 3. Indole synthesis in the side chain of amino acids or peptides
 - 3.1. Starting from δ -oxoamino acids
 - 3.2. Larock indole synthesis
 - 3.3. Based on stannylated allylglycines
 4. Substitution of Trp by C(sp²)–H activation
 5. Conclusion
- References

Exploring selenones for heterocycle synthesis**365***Francesca Marini*

1. Introduction
 2. Synthesis and properties of selenones
 3. Synthesis of heterocycles via cyclizations of selenones
 4. Synthesis or functionalization of heterocycles via Michael addition/ring closure sequences
 5. Multicomponent synthesis of 3-spirooxindole-pyrrolizines via [3+2] cycloaddition/elimination processes
 6. Conclusion and outlook
- Acknowledgement
References

Indole derivatives as core structural motifs in molecular organic photoactuators 381

Nadja A. Simeth, Stefano Crespi

1. Introduction
 2. Indigo and indigoid photoswitches
 - 2.1. Indigo, indirubin, and the peculiarity of isoindigo
 - 2.2. Hemiindigo and the related hemithioindigo
 - 2.3. Phenyliminoindolinones
 3. Feringa-type molecular motors based on oxindoles
 4. Indole-based azo-photoswitches
 5. Diarylethenes
 6. Fulgides and fulgimides
 7. Spiropyrans and merocyanine
 8. Donor acceptor Stenhouse adducts
 9. Conclusion
- Acknowledgements
- References

Synthesis of carbazoles and derivatives from allenes 409

José M. Alonso, Pedro Almendros

1. Introduction
 2. Synthesis of carbazoles and derivatives by transition metal catalysis
 - 2.1. Gold and silver catalysis
 - 2.2. Platinum catalysis
 - 2.3. Palladium catalysis
 - 2.4. Other metals
 3. Metal-free methodologies
 4. Conclusion
- Acknowledgement
- References

Annulation of 2-alkynylbenzamides: the versatile chemical compounds 424

Vaezeh Fathi Vavsari, Saeed Balalaie

1. Introduction
 2. Annulation reaction of 2-alkynylbenzamides
 - 2.1. Synthesis of five-membered heterocycles
 - 2.2. Synthesis of six-membered heterocycles
 - 2.3. Synthesis of seven-membered heterocycles
 3. Conclusions
- References

Access to five-membered N-heteroaromatic compounds: current approach on microwave-assisted synthesis 436

Maria-Celeste Ortiz, Jaime Portilla

1. Introduction
2. Pyrrole-based systems
 - 2.1. Pyrrole derivatives synthesis
 - 2.2. Aza-fused pyrroles 5:6
3. Compounds incorporating the pyrazole ring
 - 3.1. Pyrazoles synthesis
 - 3.2. Some aza-fused ring 5:6
4. Imidazole derivatives

- 4.1. Imidazoles synthesis
- 4.2. Aza-fused imidazoles 5:6
- 5. Systems bearing triazole rings
- 6. Conclusion
- Acknowledgments
- References

Chemistry of 2H-isoindoles: recent developments

463

Carmen Nájera, José M. Sansano, Miguel Yus

- 1. Introduction
- 2. Synthesis by ring-closure reactions
 - 2.1. Alkynes cyclization
 - 2.2. 1,3-Dipolar cycloadditions
 - 2.3. Intramolecular α -arylation of amino esters
 - 2.4. Cyclization of benzylamines
- 3. Synthesis by aromatization processes
 - 3.1. C–H Functionalization of isoindoles
 - 3.2. [1,5]-Hydrogen shift of isoindolines
- 4. Synthesis by ring transformation
- 5. Other reactions
- 6. Conclusion
- Acknowledgements
- References

Synthesis of functionalized heterocyclic compounds driven by visible-light photocatalysis

480

Lydia M. Bouchet, Adrián A. Heredia, Ignacio D. Lemir, Juan E. Argüello, Luciana C. Schmidt

- 1. Introduction
- 2. Benzothiazoles
 - 2.1. Synthesis by C-H activation and C(sp²)-S formation
 - 2.2. Synthesis starting from 2-aminothiophenols
 - 2.3. Synthesis starting from 2-isocyanoaryl thioethers
- 3. Triazoles
 - 3.1. Visible-light promoted copper(I)-catalysed azide-alkyne cycloaddition
 - 3.2. Visible-light assisted copper-free triazole synthesis
 - 3.3. Visible-light-driven triazole functionalization
- 4. Selenoindoles
 - 4.1. Indole ring reactivity
 - 4.2. Synthesis of 3-selenoindoles by direct irradiation
 - 4.3. Synthesis of 3-selenoindoles using photocatalysis
 - 4.4. Synthesis of fluorinated 3-selenoindoles
- 5. Conclusion
- Acknowledgement
- References

Fluorinated N-heterocycles as conformationally diverse bioactives for drug discovery

502

Fei Liu, Bilqees Sameem

- 1. Introduction
- 2. Fluorine as a conformation tuning tool
- 3. Conformation-based bioactive drug discovery as new frontiers
- 4. Common fluorination methods for C–F bond formation
- 5. Conformational tuning by fluorine substitution on piperidines
- 6. Conformational tuning by fluorine substitution on azepanes

7. Conclusion
Acknowledgements
References