#### **Table of contents**

## **Disubstituted 1,2,3-triazoles as amide bond mimetics**

Miriam Corredor, Jordi Solà and Ignacio Alfonso

- 1. Introduction
- 2. Synthesis of disubstituted 1,2,3-triazole rings
- 2.1. Synthesis of 1,4-disubstituted-1,2,3-triazoles
- 2.2. Synthesis of 1,5-disubstituted-1,2,3-triazoles
- 2.3. Synthesis of 2,4-disubstituted-1,2,3-triazoles

## 3. Structural properties

- 3.1. Physico-chemical properties of the differently substituted 1,2,3-triazoles
- 3.2. Structural characterization
- 4. Disubstituted triazole rings in peptides
- 4.1. Triazole as a peptide bond mimic
- 4.2. Cyclic peptides
- 4.3. Oligomeric triazolamers
- 5. Disubstituted triazole rings in peptoids
- 6. Conclusions
- Acknowledgements

References

## The synthesis of azahelicenes

## Ivo Starý and Irena G. Stará

- 1. Introduction
- 2. Synthesis of pyridohelicenes
- 2.1. Photochemical methodology
- 2.2. Non-photochemical methodologies
- 3. Synthesis of other azahelicenes
- 3.1. Cationic azahelicenes
- 3.2. Non-cationic azahelicenes
- 4. Nonracemic pyridohelicenes and other azahelicenes
- 4.1. Resolution of racemates
- 4.2. Asymmetric synthesis
- 5. Functionalisation of existing pyridohelicenes and other azahelicenes
- 6. Conclusions
- Acknowledgments
- References

## Advances and challenges in the synthesis of pyrrole systems of a limited access

- Dmitrii A. Shabalin, Elena Yu. Schmidt and Boris A. Trofimov
- 1. Introduction
- 2. Synthesis of 3H-pyrroles
- 2.1. Modification of 1*H*-pyrroles
- 2.2. From carbonyl compounds
- 2.3. From oximes
- 2.4. From nitriles
- 2.5. From isonitriles
- 2.6. Miscellaneous methods
- 3. Synthesis of pyrrole analogues of stilbenes
- 3.1. Nucleophilic addition to het(aryl)acetylenes
- 3.2. Syntheses from oxiranes
- 3.3. Syntheses involving transition metal complexes

54

23

## 1

3.4. Miscellaneous methods

4. Synthesis of di- and oligopyrroles separated by conjugated heterocyclic systems

List of abbreviations

References

# Construction of 1,4,6,10-tetraazaadamantanes via intramolecular oxime/hydrazine

cyclotrimerization approach Artem N. Semakin and Alexey Yu. Sukhorukov

# 1. Introduction

- 2. Synthetic strategy towards 1,4,6,10-tetraazaadamantane cage
- 3. Synthesis of tris-oximes and tris-hydrazones as precursors of 1,4,6,10-tetraazaadamantanes
- 4. Studies of the intramolecular cyclotrimerization of C=N groups in tris-oximes and tris-hydrazones

Π

- 5. Stabilization of 1,4,6,10-tetraazaadamantane cage
- 6. Synthesis of unsubstituted 1,4,6,10-tetraazaadamantane ("isourotropine") and its derivatives
- 7. Comparison of urotropine and "isourotropine" structures
- 8. Application of 1,4,6,10-tetraazaadamantanes for the design of water-soluble functional molecules
- 9. Conclusions

Acknowledgements

References

# **Quinoxaline synthesis by domino reactions**

# Jie-Ping Wan and Li Wei

# 1. Introduction

- 2. Synthesis using o-phenylenediamine as the main building blocks
- 2.1. Reaction with vicinal dicarbonyl compounds
- 2.2. Reactions with  $\alpha$ -haloketones
- 2.3. Reactions with  $\alpha$ -hydroxylated ketones and vicinal diols
- 2.4. Reactions with alkynes and alkenes
- 2.5. Reactions with methylene aldehydes and ketones
- 2.6. Reactions with other substrates
- 3. Synthesis using o-nitroanilines as o-phenylenediamine precursors
- 4. Reactions without o-phenylenediamine
- 4.1. Reactions involving aryl C-H functionalization
- 4.2. Reactions using *ortho*-diisocyanoarenes
- 4.3. Other reactions
- 5. Conclusion
- Acknowledgements

References

# Thiourea-amine catalysed asymmetric synthesis of functionalised epoxides

Sara Meninno and Alessandra Lattanzi

- 1. Introduction on bi- and multifunctional thiourea-amines
- 2. Asymmetric organocatalytic nucleophilic epoxidation overview
- 3. Thiourea-amine catalysed epoxidation of electron-poor alkenes
- 4. Thiourea-amine catalysed kinetic resolution of racemic epoxides
- 5. Conclusions
- Acknowledgements

References

# Cyclic benzoxathiazine 2,2-dioxides: versatile electrophiles for asymmetric catalysis

Lode De Muck, Carlos Vila and José R. Pedro

1. Introduction

98

124

137

- 2. Preparation of benzoxathiazine 2,2-dioxides
- 3. The use of benzoxathiazine 2,2-dioxides as electrophiles for asymmetric catalysis
  - 3.1. Addition reactions of organometallic reagents
  - 3.1.1. Addition reactions of organoboron reagents
  - 3.1.2. Addition reactions of organozinc reagents
  - 3.2. Cycloadditions reactions
  - 3.3. Mannich reactions
  - 3.4. Friedel-Crafts reactions
  - 3.5. Hydrogenation reactions
- 4. Conclusions
- Acknowledgement

References

# Recent advances in catalytic asymmetric cascade reactions of 3-isothiocyanato oxindoles158for synthesis of spirooxindoles158

Fen Tan and Hong-Gang Cheng

1. Introduction

- 2. Asymmetric aldol/cyclization cascade reaction of 3-isothiocyanato oxindoles with ketones or aldehydes
- 2.1. Aldol/cyclization cascade reaction of ketones
- 2.2. Aldol/cyclization cascade reaction of aldehydes
- 3. Asymmetric Mannich/cyclization cascade reaction of 3-isothiocyanato oxindoles with imines
- 3.1. Mannich/cyclization cascade reaction of aldimines
- 3.2. Mannich/cyclization cascade reaction of ketoimines
- 3.3. Mannich/cyclization cascade reaction of □, □-unsaturated aldimines
- 4. Asymmetric Michael/cyclization cascade reaction of 3-isothiocyanato oxindoles with electron-deficient alkenes or alkynes
- 4.1. Michael/cyclization cascade reaction of 3-ylideneoxindoles
- 4.2. Michael/cyclization cascade reaction of nitroolefins (cyclic or acyclic nitroolefins)
- 4.3. Michael/cyclization cascade reaction of 3-nitroindoles
- 4.4. Michael/cyclization cascade reaction of allenic esters or 2-butynedioic acid diesters or alkyne ketones
- 4.5. Michael/cyclization cascade reaction of miscellaneous electron-deficient alkenes
- 5. Asymmetric cascade reaction of 3-isothiocyanato oxindoles with azodicarboxylates
- 6. Asymmetric ring-opening/closing cascade reaction of 3-isothiocyanato oxindoles with aziridines
- 7. Conclusions
- Acknowledgments

References

# Recent advances in catalytic asymmetric cycloaddition reactions of *ortho*-quinone methides181for synthesis of *O*-heterocycles181

Xiao-Ye Yu, Wen-Jing Xiao and Jia-Rong Chen

1. Introduction

- 2. Catalytic asymmetric cycloaddition reactions of ortho-quinone methides
- 2.1. Lewis acid-catalyzed cycloaddition reactions
- 2.2. Phase-transfer catalytic cycloaddition reactions
- 2.3. N-Heterocyclic carbene-catalyzed cycloaddition reactions
- 2.4. Brønsted acid-catalyzed cycloaddition reactions
- 2.5. Bifunctional chiral Brønsted base catalysis
- 3. Miscellaneous
- 4. Conclusions
- Acknowledgements
- References

# Visible light-induced photocatatalytic synthesis of five-membered nitrogen heterocycles

- *Quan-Qing Zhao, Dong-Mei Yan, Jia-Rong Chen and Wen-Jing Xiao* 1. Introduction
- 2. Visible light-induced synthesis of pyrrole derivatives
- 2.1. The synthesis of pyrroles
  - 2.1.1. Visible light-induced formal [3+2] cycloaddition reaction
  - 2.1.2. Visible light-induced Hantzsch reaction
- 2.2. The synthesis of pyrrolidines and pyrrolines
- 2.2.1. Visible light-induced formal [2+2] cycloaddition reaction
- 2.2.2. Visible light-induced 1,3-dipolar cycloaddition reaction
- 2.2.3. Visible light-induced radical cyclization reaction
- 2.2.4. Visible light-induced nucleophilic cyclization reaction
- 2.3. The synthesis of pyrrolidin-2-ones
- 3. Visible light-induced synthesis of indole derivatives
- 3.1. The synthesis of indole derivatives via tandem radical cyclization
- 3.2. The synthesis of indole derivatives *via* dual catalysis
- 4. Visible light-induced synthesis of pyrazole derivatives
- 4.1. The synthesis of pyrazole derivatives via nitrogen radical cyclization
- 4.2. The synthesis of pyrazole derivatives via nucleophilic cyclization
- 5. Visible light-induced synthesis of imidazole derivatives
- 5.1. The synthesis of imidazole derivatives via formal [3+2] cyclization
- 5.2. The synthesis of imidazole derivatives via nucleophilic cyclization

6. Miscellaneous

- 6.1. Visible light-induced synthesis of thiazole derivatives
- 6.2. Visible light-induced synthesis of isoxazole derivatives

7. Conclusions

Acknowledgments

References

## Cycloadditions with mesoionic dipoles: strategy and control

- Juan García de la Concepción, R. Fernando Martínez, Pedro Cintas and José L. Jiménez
- 1. Introduction and scope
- 2. Sydnones
- 2.1. Cycloaddition of sydnones with alkynes
- 2.1.1. Conventional cycloadditions
- 2.1.2. Activated cycloadditions
- 2.1.3. Application in bioorthogonal chemistry
- 2.2. Cycloaddition of sydnones with alkenes
- 2.3. Preparation of polymeric materials
- 3. Münchnones
  - 3.1. Synthesis and cycloadditions with alkynes
  - 3.2. Cycloadditions with alkenes.
  - 3.3. Other reactions of münchnones
- 3.4. Phospha-münchnones
- 4. Isomünchnones and thioisomünchnones
- 5. Other mesoionic dipoles
- 5.1. 1,2-Diazoimines
- 5.2. 1,2-Dithiol-4-ones
- 5.3. 1,3-Diazol-4-ones
- 5.4. 1,3-Oxazol-5-imines
- 6. Conclusions
- Acknowledgement

# References

## Pd and Cu-mediated domino reactions for the synthesis of sulfur heterocycles 254 Morgan Donnard, Thomas Castanheiro and Mihaela Gulea 1. Introduction 2. Synthesis of heterocycles incorporating only sulfur heteroatom 2.1. From sulfur-containing starting material 2.2. From sulfur-free starting material 3. Synthesis of heterocycles incorporating one sulfur and at least another heteroatom 3.1. N,S-Heterocycles 3.1.1. From sulfur-containing starting material 3.1.2 From sulfur-free starting material 3.2 O,S-Heterocycles 3.2.1. From sulfur-containing starting material 3.2.2. From sulfur-free starting material 4. Conclusion Acknowledgements References 2,3-Methanopyrrolidines: synthesis and ring-opening transformations 277 Yvan Six 1. Introduction 2. Methods of preparation 2.1. Cyclopropanation of 2-pyrroline derivatives 2.2. Intramolecular cyclopropanation of N-homoallylamine derivatives 2.3. Intramolecular cyclopropanation of enamine derivatives 2.4. Transannular cyclisation 2.5. Formation of the cyclopropane ring from a pyrrolidine precursor 2.6. Pyrrolidine ring-closure from an aminocyclopropane precursor 2.7. Miscellaneous methods 3. Transformation into other nitrogen-containing heterocyclic systems 3.1. Cyclisation of an iminium intermediate generated by protonation 3.2. Isomerisation into an enamine intermediate and subsequent transformations 3.3. 1,3-Dipolar cycloaddition taking place after isomerisation into an azomethine ylid 3.4. Single-electron oxidation followed by formal [3+2] cycloaddition 3.5. Ring expansion of 2-halo-1-aminocyclopropane derivatives 3.6. Miscellaneous transformations Acknowledgements References

308

## Synthetic approaches towards 2-spiropseudoindoxyls

Niels Marien, B. Narendraprasad Reddy and Guido Verniest

- 1. Introduction
- 2. Synthetic approaches towards pseudoindoxyls
- 3. Oxidations of fused indoles
- 4. Indol-3-ones as starting material
- 5. Indoleninones as starting material or key intermediate
- 6. Cycloadditions with isatogens
- 7. Formation of the indol-3-one five-membered ring
- 8. Conclusion
- Acknowledgements
- References

## **Recent advances in aminopyrazoles synthesis and functionalization**

Jeanne Fichez, Patricia Busca and Guillaume Prestat

1. Introduction

- 2. Synthesis of 3-(5)-aminopyrazoles
- 2.1. Reaction of  $\beta$ -ketonitriles with hydrazines
  - 2.1.1. With the hydrazine
- 2.1.2. With monosubstituted hydrazines
- 2.2. Condensation of  $\alpha$ , $\beta$ -unsaturated nitriles with hydrazines
  - 2.2.1. With the hydrazine
- 2.2.2. With monosubstituted hydrazines
- 2.3. Miscellaneous
  - 2.3.1. Synthesis of aminopyrazoles from isoxazoles
  - 2.3.2. Synthesis of aminopyrazoles from isothiazoles
- 3. Synthesis of 4-aminopyrazoles
- 3.1. Knorr pyrazole synthesis
- 3.2. Reaction of hydrazine with  $\alpha$ , $\beta$ -unsaturated ketones
- 3.3. Thorpe-Ziegler cyclization
- 4. Mono-functionalization of aminopyrazoles
- 4.1. Transition-metal-catalyzed C-H functionalization of aminopyrazole
- 4.2. Transition-metal-catalyzed *N*-arylation of aminopyrazoles
- 4.2.1. Palladium-catalyzed *N*-arylation with biased aminopyrazoles
- 4.2.2. Palladium-catalyzed N-arylation with unbiased aminopyrazoles
- 4.2.3. Copper-catalyzed N-arylation with biased aminopyrazoles
- 4.2.4. Copper-catalyzed N-arylation with unbiased aminopyrazoles
- 4.2.5. Nickel-catalyzed N-arylation with unbiased aminopyrazoles
- 4.3. Conclusion
- 5. Di-functionalization of aminopyrazoles
- 5.1. General trends of chemical reactivity
- 5.2. Formation of pyrazolo[1,5-*a*]pyrimidines
  - 5.2.1. Reaction with  $\beta$ -diketones
  - 5.2.2. Reaction with activated enones
  - 5.2.3. Reaction with acrylonitriles
  - 5.2.4. Miscellaneous
- 5.3. Formation of pyrazolo[3,4-b]pyridines
  - 5.3.1. Reaction with  $\beta$ -diketones
- 5.3.2. Reaction with activated enone
- 5.3.3. Reaction with chromones
- 5.3.4. MCR with aldehyde and ketone
- 5.3.5. MCR with aldehyde and dicarbonyl reagent
- 5.3.6. MCR with aldehyde and 3-oxo-propanenitrile
- 5.3.7. Miscellaneous
- References

## Atropisomeric bis-heterocycles as chiral pools for asymmetric transformations

- Fabrizio Pertusati
- 1. Introduction
- 1.1. Atropisomerism
- 1.2. N-N Atropisomers
- 1.3. Atropisomeric N,N-bisazaheterocycles
- 2. 3,3'-Biquinazoline-4,4'-diones (BiQs)
- 2.1. Atropisomerism in 2,2'-disubstituted-3,3'-biquinazoline-4,4'-diones
- 2.2. Synthesis of symmetrical 2,2'-disubstituted-3,3'-biquinazoline-4,4'-diones

372

- 2.3. Synthesis of unsymmetrical 2,2'-disubstituted-3,3'-biquinazoline-4,4'-diones
- 2.3.1. Synthesis of 2-alkyl-3-aminoquinazoline-4(3H)-ones
- 2.3.2. Synthesis of 4H-3,1-benzoxazine-4-ones
- 2.3.3. Synthesis of unsymmetrical 2,2'-disubstituted-3,3'-biquinozaline-4,4'-diones *via* condensation of 3-aminoquinozaline-4(3*H*)-ones and 4*H*-3,1-benzoxazine-4-ones
- 2.4. Synthesis of 2-chirally-substituted-3,3'-biquinazoline-4,4'-diones.
- 2.5. Synthesis of 2,2'-chirally-substituted-3,3'-biquinazoline-4,4'-diones
- 3. Functionalization of symmetrical BiQ and their substrate controlled asymmetric reactions
- 3.1. Substrate controlled reactions of 2,2'-disubstituted-3,3'-biquinazoline-4,4'-diones
- 3.2. Attempt to remove the newly formed chiral center
- 4. Conclusions and further work
- Acknowledgment

References

## Synthesis of 1,4-benzoxathiin-9H-purine derivatives as antiproliferative agents

- Olga Cruz-López, Joaquín M. Campos and Ana Conejo-García
- 1. Introduction
- 2. 9-(2,3-Dihydro-1,4-benzoxathiin-3-ylmethyl)-9H-purines
- 2.1. Synthesis
- 2.2. Biological assays
- 3. 9-(2,3-Dihydro-1,4-benzoxathiin-2-ylmethyl)-9H-purines
- 3.1. Synthesis
- 3.2. Biological assays
- 4. (R)- and (S)-9-(2,3-Dihydro-1,4-benzoxathiin-3-yl and 2-ylmethyl)-9H-purines
- 4.1. Synthesis
- 4.2. Biological assays
- 5. Conclusions
- Acknowledgement
- References

Synthesis of fused aromatic N-heterocycles by tandem site-selective palladium-catalyzed	389
C-C and C-N coupling reactions	

Tran Quang Hung, Tuan Thanh Dang, Nghia Ngo Pham and Peter Langer

- 1. Introduction
- 2. Synthesis of fused N-heterocycles based on tandem Pd-catalyzed C-C and C-N coupling reactions
- 3. Synthesis of fused N-heterocycles based on tandem Pd-catalyzed C-N coupling and C-H activation
- 4. Synthesis of fused N-heterocycles based on tandem double Pd-catalyzed C-N coupling reactions
- 5. Conclusions and perspectives

References