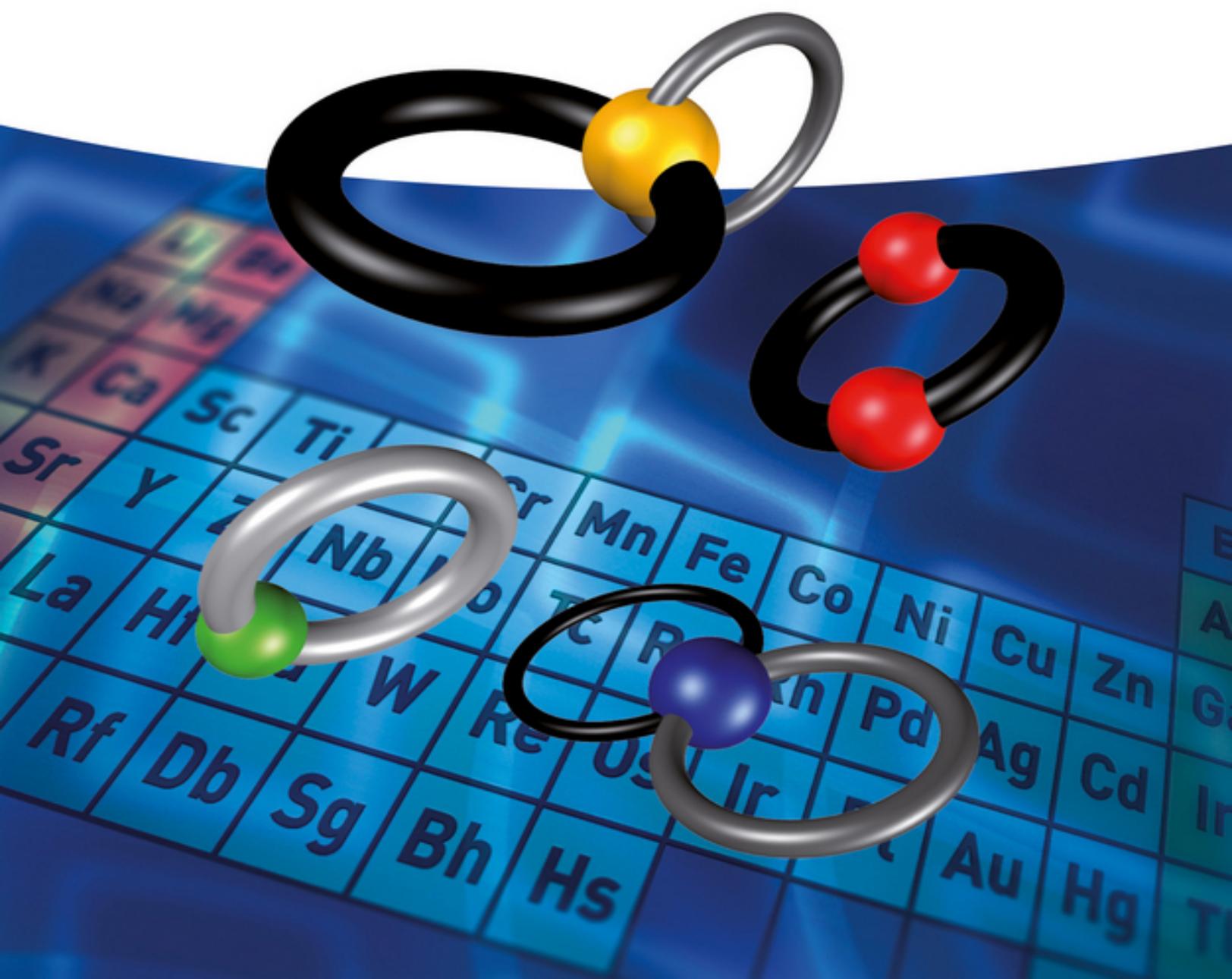


Edited by Xiao-Feng Wu

# Transition Metal-Catalyzed Heterocycle Synthesis via C-H Activation



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## Chapter 5: Rh-Catalyzed Synthesis of Nitrogen-Containing Heterocycles

[Scheme 5.1 A possible mechanism for the synthesis of \*N\*-heterocycles by C–H bond activation.](#)

[Scheme 5.2 Proposed catalytic mechanism for indole formation.](#)

## Chapter 6: Rh-Catalyzed Synthesis of Oxygen-Containing Heterocycles

[Scheme 6.1 Selected examples of natural products, pharmaceuticals, and biologically active compounds with oxygen-containing heterocycles.](#)

[Scheme 6.2 \(a\) Synthesis of 3-substituted phthalides from aldehydes and aromatic acids and \(b\) synthesis of 3-alkylidenephthalides from benzoic acids.](#)

[Scheme 6.3 Synthesis of phthalides from benzimidates and aldehydes.](#)

[Scheme 6.4 Synthesis of phthalides by oxidative coupling of aldehydes.](#)

[Scheme 6.5 Synthesis of benzofurans from \*N\*-phenoxyacetamides and alkynes.](#)

Scheme 6.6 Synthesis of furans via Rh(III)-catalyzed alkenyl C–H functionalization.

Scheme 6.7 Dehydrogenative Heck reaction of salicylaldehydes with electron-deficient olefins.

Scheme 6.8 Mechanism studies.

Scheme 6.9 Synthesis of benzoxaphosphole 1-oxides from arylphosphonic acid monoethyl esters and alkenes.

Scheme 6.10 Synthesis of dihydrobenzofuro[2,3-d]oxazoles from aryloxyacetamide and alkynes.

Scheme 6.11 Synthesis of dihydrobenzofuran via Rh(III)-catalyzed C–H functionalization of aromatic imines with tethered 1,1-disubstituted alkenes by Rovis. (a) Mechanistic hypothesis; (b) Rh(III)-catalyzed intramolecular hydroarylation; and (c) Rh(III)-catalyzed intramolecular amidoarylation.

Scheme 6.12 Rh(III)-catalyzed intramolecular amidoarylations by Glorius.

Scheme 6.13 Synthesis of chiral dihydrobenzofurans via Rh(III)-catalyzed enantioselective hydroarylation.

Scheme 6.14 Synthesis of dibenzofuran via decarbonylative C–H arylation of 2-aryloxybenzoic acids.

Scheme 6.15 Synthesis of naphtho[1,8-*bc*]pyran derivatives from 1-naphthols and alkynes.

Scheme 6.16 Synthesis of isochromenes by oxidative annulation of benzyl alcohols with alkynes by Miura and Tanaka.

Scheme 6.17 Synthesis of naphtho[1,8-*bc*]pyrans via Rh(III)-catalyzed oxidative coupling of substituted benzoylacetone nitriles with alkynes.

Scheme 6.18 Synthesis of benzopyrans from 2-aryl-3-hydroxy-2-cyclohexenone.

Scheme 6.19 Synthesis of tetracyclic naphthoxazoles from naphthoquinone.

Scheme 6.20 Synthesis of 2*H*-chromene via rhodium(III)-catalyzed annulation of cyclopropenes with *N*-phenoxyacetamides.

Scheme 6.21 Proposed mechanism.

Scheme 6.22 Synthesis of 2,2-disubstituted 2*H*-chromenes from 2-alkenylphenols and allenes.

Scheme 6.23 (a) Synthesis 2,3-disubstituted chromones by oxidative coupling between salicylaldehydes and internal alkynes by Miura and Satoh and (b) synthesis of chromone and chromane from salicylaldehyde and styrene by Glorius.

Scheme 6.24 (a) Synthesis of 3,4-diphenylisocoumarin via oxidative coupling of benzoic acids with alkynes; (b) synthesis of 3,4-diphenylisocoumarin under air; (c) synthesis of functionalized  $\alpha$ -pyrone by oxidative coupling of substituted acrylic acids with alkynes; and (d) synthesis of 3-substituted isocoumarins from benzoic acids and geminal-substituted vinyl acetates.

Scheme 6.25 (a) Synthesis of phosphaisocoumarins from phenylphosphinic acids and (b) synthesis of phosphaisocoumarins from arylphosphonic acid monoesters.

Scheme 6.26 Synthesis of isocoumarins from *N,N*-diethyl-*O*-benzoylhydroxylamine and alkynes.

Scheme 6.27 Synthesis of (4-benzylidene)isochroman-1-ones from benzamides and propargyl alcohols.

[Scheme 6.28 Synthesis of diverse bisheterocycles.](#)

[Scheme 6.29 Synthesis of dihydropyrans from acetylenic sulfones.](#)

[Scheme 6.30 Synthesis of dihydrobenzopyrans via intramolecular hydroarylation or amidoarylation. \(a\) Intermolecular hydroarylation; \(b\) intermolecular amidoarylation; and \(c\) intermolecular Heck-type reaction.](#)

[Scheme 6.31 Synthesis benzoxepines via Rh\(III\)-catalyzed annulation of \*o\*-vinylphenols with alkynes.](#)

[Scheme 6.32 Synthesis of 1,2-oxazepines from \*N\*-phenoxyacetamides and  \$\alpha,\beta\$ -unsaturated aldehydes.](#)

[Scheme 6.33 Synthesis of 3,4-fused indole skeletons via intramolecular cyclization of tethered alkynes.](#)

## Chapter 7: Ruthenium-Catalyzed Synthesis of Heterocycles via C–H Bond Activation

[Scheme 7.1 Proposed mechanism for ruthenium-catalyzed indole synthesis from 2,6-xylylisocyanides.](#)

[Scheme 7.2 Proposed mechanism for ruthenium-catalyzed pyrrolidone synthesis from allylic formamides.](#)

[Scheme 7.3 Proposed mechanism for ruthenium-catalyzed intramolecular olefin hydrocarbamylation through direct activation of the formyl C–H bond.](#)

[Scheme 7.4 Proposed mechanism for ruthenium-catalyzed intramolecular olefin hydrocarbamylation through initial activation of the N–H bond.](#)

[Scheme 7.5 Proposed mechanism for ruthenium-catalyzed benzofuran synthesis from \*N\*-phenoxy-pivalamide.](#)

[Scheme 7.6 Proposed mechanism for ruthenium-catalyzed cyclocarbonylation of yne-aldehydes.](#)

[Scheme 7.7 Proposed mechanism for ruthenium-catalyzed cyclization of amines with alkynes.](#)

[Scheme 7.8 Proposed mechanism for ruthenium-catalyzed cyclization of benzamides with alkynes.](#)

[Scheme 7.9 Proposed mechanism for ruthenium-catalyzed oxidative annulations of isoquinolones with alkynes.](#)

[Scheme 7.10 Proposed mechanism for ruthenium-catalyzed 3-\(1\*H\*-indol-1-yl\)propanamide synthesis from phenylpyrazolidin-3-ones.](#)

[Scheme 7.11 Proposed mechanism for ruthenium-catalyzed oxidative alkenylation and cyclization of \*N\*-methoxybenzamides.](#)

[Scheme 7.12 Proposed mechanism for ruthenium-catalyzed oxidative alkenylation and cyclization of aromatic nitriles.](#)

[Scheme 7.13 Proposed mechanism for ruthenium-catalyzed three-component coupling reaction of  \$\alpha,\beta\$ -unsaturated imines with CO and alkenes.](#)

[Scheme 7.14 Proposed mechanism for ruthenium-catalyzed carbonylation and cyclization of aliphatic amides.](#)

## Chapter 8: Cu-Catalyzed Heterocycle Synthesis

[Scheme 8.1 Cu\(OAc\)<sub>2</sub> catalyzed lactams formation using 5-methoxyquinolyl as directing group.](#)

[Scheme 8.2 CuCl catalyzed lactams formation using 5-methoxyquinolyl as directing group.](#)

Scheme 8.3 CuI catalyzed synthesis of 2-monosubstituted and 2,5-disubstituted pyrroles.

Scheme 8.4 Cu(OAc)<sub>2</sub> catalyzed synthesis of 3-Azabicyclo[3.1.0] hex-2-enes and 4-carbonylpyrroles.

Scheme 8.5 CuI catalyzed synthesis of polysubstituted pyrroles.

Scheme 8.6 Copper catalyzed synthesis of 2,3,4-trisubstituted pyrroles.

Scheme 8.7 The regiocontrolled formation of pyrroles via a formal [3+2] cycloaddition of isocyanides and electron-deficient alkynes.

Scheme 8.8 Cu(NTf<sub>2</sub>)<sub>2</sub>-catalyzed synthesis of pyrroles from ethoxycarbonyl vinyl azides and ethyl acetoacetate.

Scheme 8.9 CuOTf-catalyzed synthesis of polysubstituted pyrroles from diazoketones, nitroalkenes, and amines.

Scheme 8.10 Cu(OAc)<sub>2</sub>-promoted oxidative coupling of enamides with electron-deficient alkynes for the synthesis of multisubstituted NH pyrroles.

Scheme 8.11 CuPF<sub>6</sub>-catalyzed pyrrolidines formation via radical aminohydroxylation of double bonds of unsaturated N-benzoyloxyamines.

Scheme 8.12 A Cu-Xantphos system for the synthesis of pyrrolidine and piperidine derivatives.

Scheme 8.13 Intramolecular diastereoselective aminoxygenation of unactivated alkenes to pyrrolidines.

Scheme 8.14 Copper catalyzed synthesis of 2-chloromethylpyrrolidines.

2-substituted benzothiazoles  
9-substituted xanthene synthesis  
sugar-based benzothiazoles  
sulfamoyl azide catalysis  
4-sulfonamidoquinolines  
sulfonylmethyl isocyanide  
sulfur-bridged polycycles  
sulfur-containing heterocycles

Pd-catalyzed synthesis

benzo[*b*]thiophenes

benzothiazoles

sultams

sultones

sultams

sultones

surface-modified TiO<sub>2</sub>

***t***

TBDPS-protected *o*-bromophenols

tertiary alcohol

tertiary amines

radical cyclization

visible-light-induced radical cyclization

tertiary anilines

tetrabutylammonium bromide (TBAB)

tetracyclic naphthoxazole synthesis

tetrahydroazepin  
tetrahydrobenz[*b*]azepin-4-ones  
tetrahydrofuran  
tetrahydrooxepin  
tetrahydroquinolines  
tetramethylaminopyridyl radical (TEMPO)  
texaline  
1,2,3-triazoles  
thiazoles  
    annuloline and siphonazole  
    JNK3 inhibitors  
    texaline, febuxostat and muscoride  
    tyrosine kinase inhibitor  
thiophenes  
2-thiophenyl derivative  
thiophenoazepinones  
three-phase tests  
tipifarnib  
triarylphosphines  
1,2,3-triazoles  
tricyclic furan  
tricyclic indole  
tricyclic pyrroles  
tricyclic sultone  
tricyclic thiophene

trifluoroacetimidoyl chlorides

trifluoromethyl (CF<sub>3</sub>) group

2-trifluoromethylbenzothiazoles

trifluoromethylation

CuI catalysis

oxindole synthesis

1,2,4-trisubstituted imidazoles

2,3,4-trisubstituted pyrroles

tunable silver-catalyzed C(sp<sub>3</sub>)–H amination method

tyrosine kinase inhibitor

## **u**

unfunctionalized olefins

unprotected compounds

indoles

ortho-aryl anilines

phenols

primary amines

## **v**

vasicoline

δ-viniferin synthesis

vinyl arenas

enantioselective carboetherification reaction

Pd-catalyzed oxidative coupling

vinyl halides

visible light-induced photocatalysis

*de novo* synthesis, heterocycles

sp<sup>2</sup>C–H functionalization

sp<sup>3</sup>C–H functionalization

direct C–H functionalization, heteroarenes

alkylation

arylation

heteroatomlation

mechanism profile

**w**

White's allylic C–H activation

**x**

xanthone derivatives

copper catalyzed synthesis

Pd catalyzed synthesis

**y**

yne-aldehydes

**z**

Zhang's procedure