Heteroatom Chemistry
Volume 14, Number 7, 2003

Oxidative Cyclization in the Synthesis of 5- and 6-Membered *N*,*O*-Heterocycles

Petros G. Tsoungas[1] and Andreas I. Diplas[2]

[1]*Department of Research and Technology, Ministry of Development, Messogion Avenue 14-18, Athens, GR-11510, Greece*

[2]*Laboratory of Pharmaceutical Chemistry, Department of Pharmacy, School of Health Sciences, University of Patras, Patras, GR-26500, Greece*

Received 2 June 2003

ABSTRACT: *The versatility and potential of oxidative cyclization in the synthesis of 5- and 6-membered N- and/or O-heterocycles is presented through judiciously selected examples.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:642–670, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10200

INTRODUCTION

Oxidative cyclization is one of the commonly used methods for ring closure [1–4]. Accordingly, annulation of suitably substituted acyclic structures give rise to diverse carbo(hetero)cyclic frameworks via this reaction. Appropriately disposed reacting sites on the substrate, other functionalities elsewhere on the structure able to survive the oxidation conditions, and the nature of the oxidizing agent are the fundamental requisites for the success of the reaction. Its entropically favored intramolecular variant is the most abundant and a well-documented C—C or C—X (X = N, O) bond-forming process [1–3]. The features of oxidative cyclization have been treated in major works of a broader theme [1,3–5].

The impressive developments in organic synthesis over the past two decades have had their share of impact on the reaction. Most notable is the versatility of the reaction when triggered or catalyzed by main group [6], lanthanide [7], or transition-metal complexes [8–18]. A plethora of diverse structures of varying complexity have been and continue to be prepared by careful selection of the metal complex and design of the substrate substitution pattern. Scattered examples of the reaction, using a wide variety of reagents, are included in the works already mentioned earlier as well as in other major references [19]. Not surprisingly, therefore, it is clear that there is a sizeable literature on the subject of potential to synthesis, a dominant part of which is focused on heterocycles.

It is the aim of this article to highlight the main features of the reaction through selected examples unveiling its versatility and potential to the synthesis of diverse 5- and 6-membered *N*- and/or *O*-heterocyclic structures. These rings are the most important ones, either suitably substituted or as units of larger more complex frameworks, in studies of biological and/or pharmacological activity [20].

The size of the literature, a phenomenon, in fact, common to every field, nowadays, dictated a judicious and selective approach to the subject. Thus literature covered is that of 1990 to date and earlier cases are included where deemed necessary.

The reaction, as exemplified in the present account, is a useful constituent of RAS (rapid analogue synthesis) methodology [21]. Combinatorial synthesis or library generation aspects [22–24] have not been included.

Dedicated to Dr. A. J. Boulton with respect and affection.

Correspondence to: Petros G. Tsoungas; e-mail: pgt@gsrt.gr.

Oxidation is taken as usually defined [25], for the overall outcome of the reaction. *Cyclization,* on the other hand, refers strictly to the ring-forming step of a reaction sequence leading to the oxidized structure. The latter may (or may not) be the final product. It also may or may not be isolable.

Cyclization embraces two main processes: (a) a reagent-triggered cyclization and (b) a spontaneous cyclization following an oxidation step (e.g. nitrile oxide dimerization or a 6π-electrocyclization).

Accordingly, besides the "conventional" dehydrogenation, other reactions covered include acid-catalyzed, electrochemical, and metal (main group, lanthanide, or transition metal)-mediated/catalyzed cyclizations.

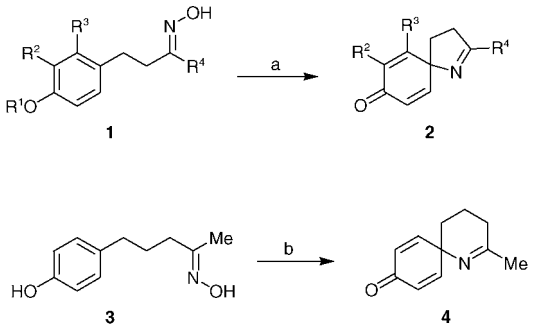
In making up this account attention has been drawn to the range and mode of action of the oxidants used for the transformation rather than the product heterocycles. Consequently the presentation is reagent-based and arranged accordingly for the sake of simplicity and clarity.

Concepts such as efficiency, atom economy, and cost-effectiveness coupled with environmental concerns [23], inevitably imposing constraints for "cleaner" processes, nowadays, are exemplified throughout the account as they have developed over the years.

ACID-CATALYZED CYCLIZATION

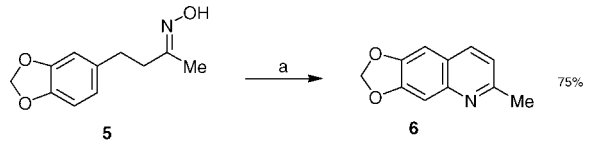
Trifluoroacetic acid (TFA)-triggered spirocyclization of oximes **1** or **2** to **3** or **4** respectively has been effected in the presence of Bu_4NReO_4 (Scheme 1) [26].

Interestingly, the quinoline **6**, isolated as a minor product (4–7%) in the above reaction, may become the major product by changing the reaction conditions (Scheme 2) [27].



a. 20 mol% Bu_4NReO_4, 100 mol% CF_3SO_3H, $ClCH_2CH_2Cl$, reflux 1-2 h
b. 20 mol% Bu_4NReO_4, 100 mol% CF_3SO_3H, CH_3NO_2, reflux 2 h

SCHEME 1



a. 20 mol% Bu_4NReO_4, 100 mol% CF_3SO_3H, 50 mol% 4-chloranil, $ClCH_2CH_2Cl$, MS 5A, reflux 1 h

SCHEME 2

ELECTROCHEMICALLY INDUCED CYCLIZATION

Anodic oxidation provides an effective access to cyclic structures. Thus, it has been successfully applied to the spirocyclization of phenol derivatives **7** (Scheme 3) [28].

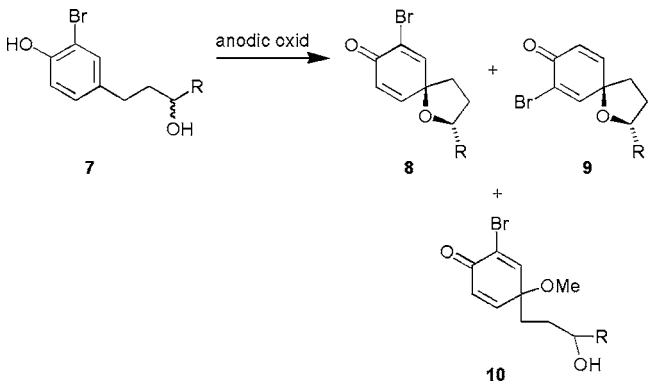
α-Stannyl ethers and carbamates with C=C bonds can also be cyclized in the presence of Bu_4NBF_4 [29] or Bu_4NClO_4—CH_2Br_2 [30] as a supporting electrolyte.

In either case the supporting electrolyte is the "electroauxiliary," which actuates the organic substrate toward electrochemical oxidation and controls the reaction pathways [31]. α-Silyl ethers effect an analogous cyclization [32].

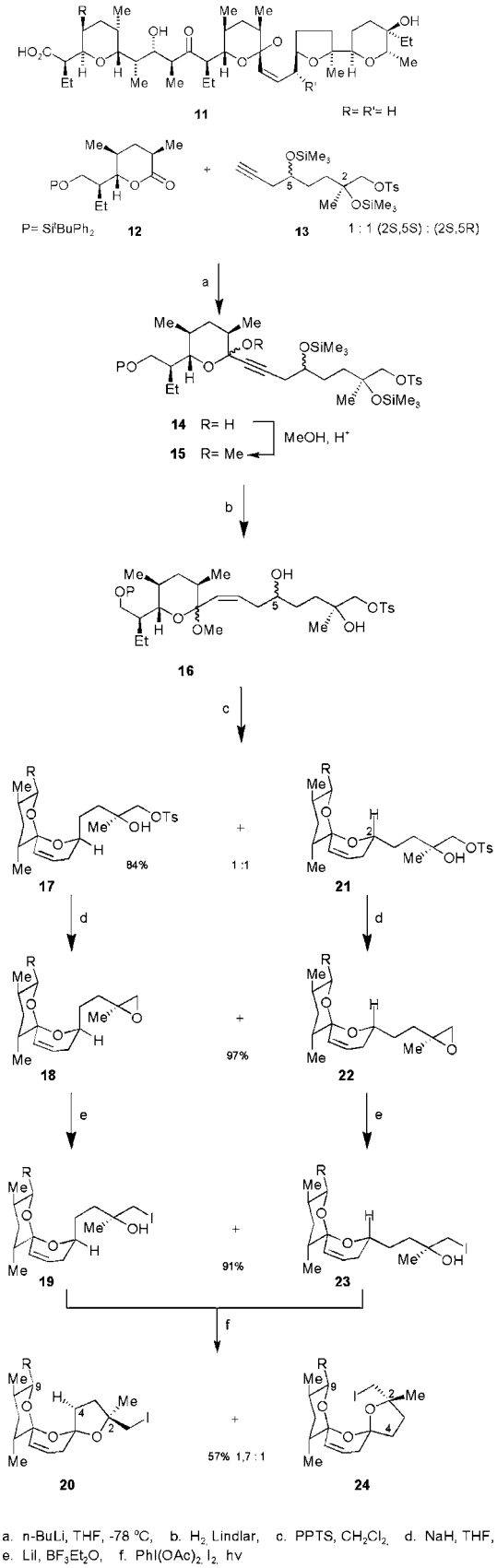
HYPERVALENT IODINE(III)-INDUCED CYCLIZATION

Hypervalent iodine-based reagents such as phenyliodine diacetate (PIDA), its trifluoro derivative (PIFA), and Dess–Martin periodinane (DMP) are commonly employed two-electron oxidants [33]. They are among the derivatives of higher valent *p*-block elements operating by the ligand coupling mechanism (see also later) [34].

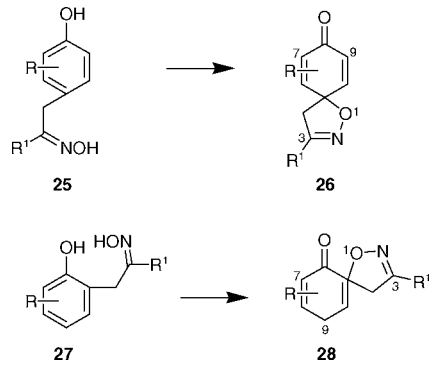
The spiroacetal moiety of the antibiotic **11** is obtained by the PIDA cyclization of spiroacetals **20** and **24** under photolytic conditions (Scheme 4) [35].



SCHEME 3



SCHEME 4



SCHEME 5

Intramolecular *o*- and *p*-spirocyclization of ketoximes **25** and **27** with PIFA leads to spiroisoxazolines **26** and **28** (Scheme 5) [36]. Other oxidants have also been used [37].

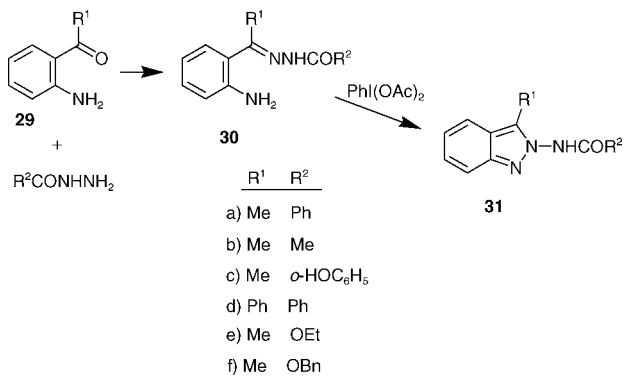
A variety of other spirocyclic structures have also been reported with hypervalent iodine oxidants [38,39]. *N*-2-Substituted indazoles **31** have been obtained by PIDA cyclization of acyl hydrazones **30** (Scheme 6) [40].

N-Acyl-hydrazones **32** are cyclized by PIDA to Δ^3-1,3,4-oxadiazolines **33** in excellent yields (Scheme 7) [41].

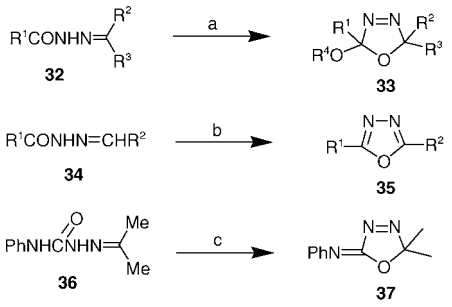
Hydrazones **34**, on the other hand, when treated with PIDA in methanolic sodium acetate give rise to 1,3,4-oxadiazoles **35** in good yields. Semicarbazones **36**, under similar conditions, give 1,3,4-oxadiazolines **37** in excellent yields too.

Phenolic Schiff bases **38**, when subjected to PIDA treatment, are cyclized to oxazoles **40** (Scheme 8) [42].

Other oxidants such as barium manganate [43], lead tetracetate [44], nickel peroxide [45], copper(I) chloride in the presence of dioxygen [46], or



SCHEME 6



a. PhI(OAc)$_2$, R^{4}OH, 0 °C. b. PhI(OAc)$_2$, r.t. c. PhI(OAc)$_2$, MeOH, 0 °C

SCHEME 7

thianthrene cation radical [47] have been used for this cyclization. Interestingly, the cyclization appears to take precedence over a rearrangement to an acylal derivative.

Hydrazones **41** have been cyclized to 1,2,3-triazoles **42** by oxidation with PIDA (Scheme 9) [48].

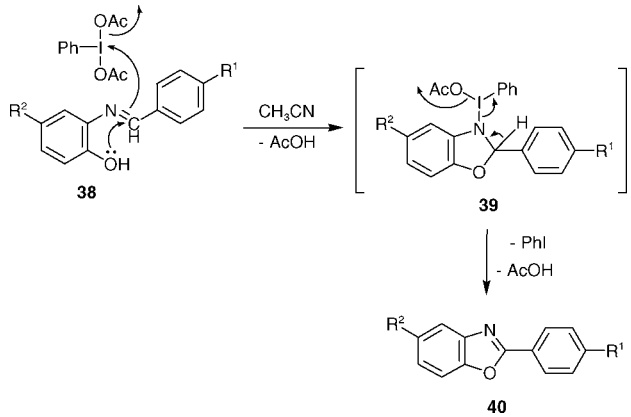
The scheme has been extended to the synthesis of various heterocycles (Scheme 10) [48].

[Hydroxy(tosyloxy)iodo]benzene (HTIB), a variant of PIDA, has been found to be effective in the oxidative cyclization of 1,3-diketone hydrazones **47** to pyrazoles **50** (Scheme 11) [49].

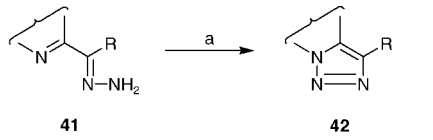
The key step in the reaction is the direct tosyloxylation of the acetyl C atom (Scheme 11).

An extensive work on the synthesis of chromenes and chromen-6-ones has been reported [50]. The scheme makes use of phenol oxidation by either PIDA or PIFA giving rise to polycyclic structures **53, 59**, or **61**, respectively (Scheme 12).

N,O-Heterocycles **66** and **68, 70, 72** have been obtained by oxidative ring closure of amides **62, 67, 69** and **71** (Scheme 13) [51].



SCHEME 8



a. PhI(OAc)$_2$, CH_2Cl_2 R= H, Me, Ph, etc.

SCHEME 9

It has been proposed that the reaction proceeds by way of a PIFA-triggered Hoffmann rearrangement, followed by cyclization of the isocyanate intermediate **64**. γ-Hydroxybutyramides **62** yield 1,3-oxazin-2-ones **66**. 3-Hydroxypropionamides **67, 69**, and **71** give 2-oxazolidin-2-ones **68, 70**, and **72** respectively. The intramolecular cyclization in both cases, being an entropically favored process, appears to be preferred over the intermolecular hydrolysis to **65**.

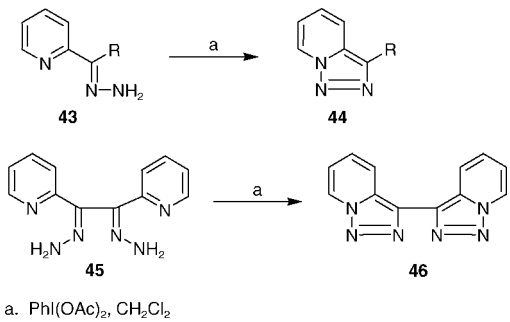
An interesting reaction sequence toward benzo[*b*]pyrans has been reported [52]. Compound **75** undergoes a PIDA oxidation to **76**, followed by spontaneous cyclization to **77** (Scheme 14).

PIDA has been an effective oxidant for the cyclization of carbamates **78** and **80** to oxazolidinones **79** and **81** in the presence of a Rh(II) carboxylate complex (Scheme 15) [53].

Besides its significance as a facile access to these heterocycles, the scheme is important for the synthesis of 1,2-amino alcohols by hydrolysis of **79** or **81** [54,55].

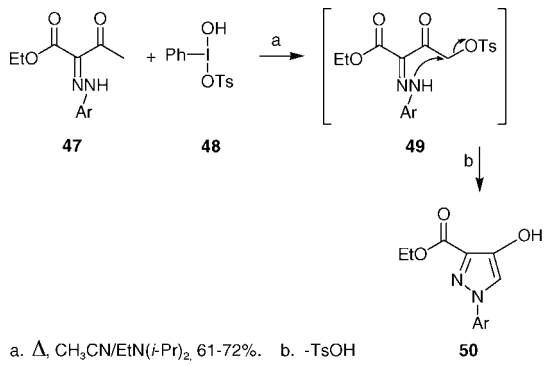
1,2,3-Triazole fused heterocycles have been prepared by PIDA-mediated oxidation of *N*-heterocyclic hydrazones [56]. The reagent has also been used for the synthesis of 1,3,4-oxadiazole and Δ^3-1,3,4-oxadiazoline derivatives from *N*-acyl-hydrazones and *N*-phenylsemicarbazones [57].

Cyclic enecarbamates **85** or **87** [58] have been obtained via an efficient tandem oxidative cyclization–dehydration of ω-hydroxycarbamates **82** or **86**, using DMP [59] (Scheme 16) [60].



a. PhI(OAc)$_2$, CH_2Cl_2

SCHEME 10

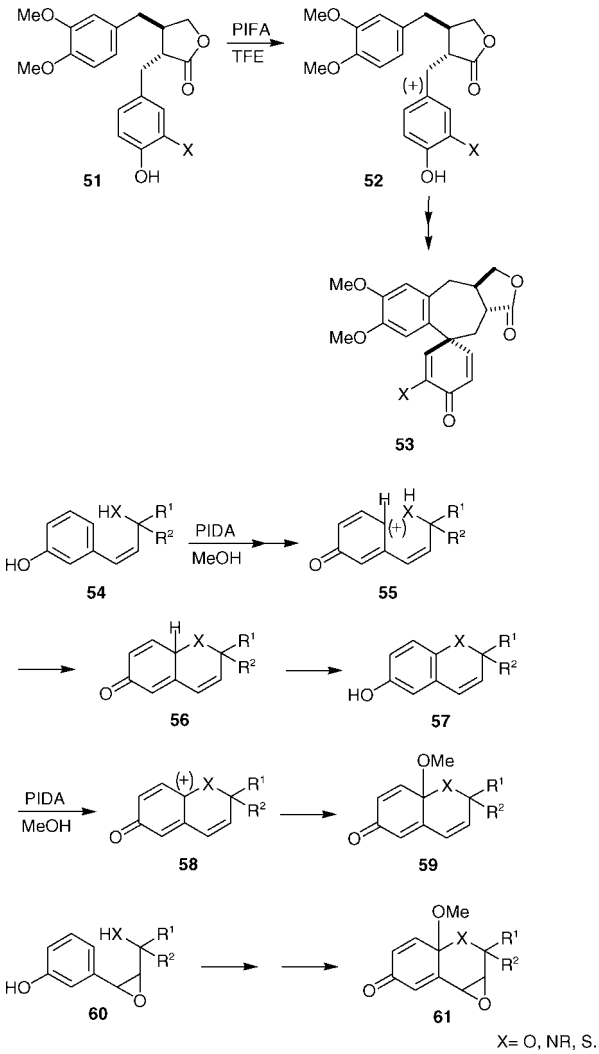


a. Δ, $CH_3CN/EtN(i\text{-}Pr)_2$, 61-72%. b. -TsOH

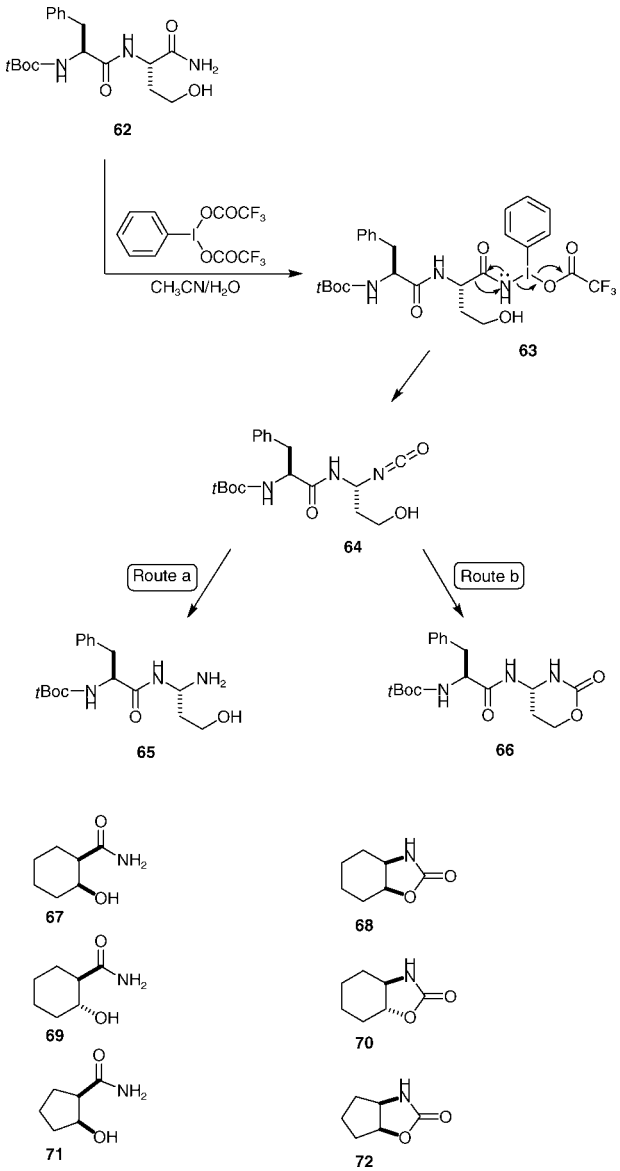
SCHEME 11

Aldehyde **88** can be cyclodehydrated to **87** by acid treatment. PIFA-induced aryl oxidative coupling has been reported (Scheme 17) [61].

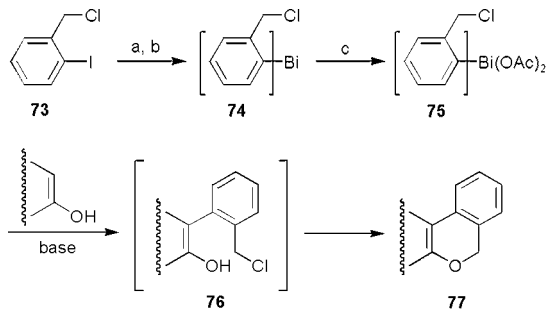
DMP has been effective in the cyclization of unsaturated *N*-aryl amides **93** or **95** to the tetracyclic



SCHEME 12

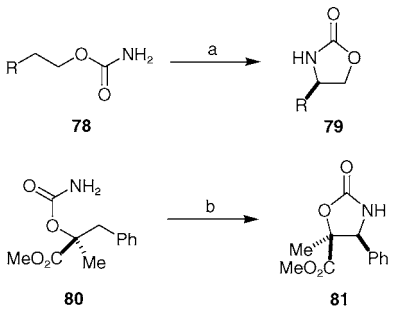


SCHEME 13



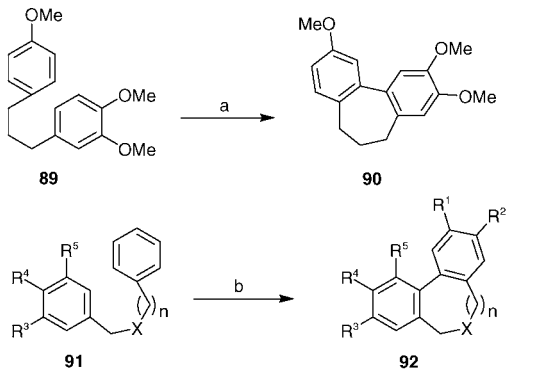
a. *i*-PrMgBr, THF, -10 °C, 3h. b. $BiCl_3$, -10 °C, 2h, then rt overnight.
c. $PhI(OAc)_2$, CH_2Cl_2.

SCHEME 14



a. 5 mol% $[Rh_2(O_2CR')_4]$, $PhI(OAc)_2$, MgO, CH_2Cl_2, 40 °C.
b. catalyst, $PhI(OAc)_2$

SCHEME 15



a. $Ph(OCOCF_3)_2$, (PIFA), solvent. b. PIFA, $BF_3.Et_2O$, CH_2Cl_2, -40 °C

SCHEME 17

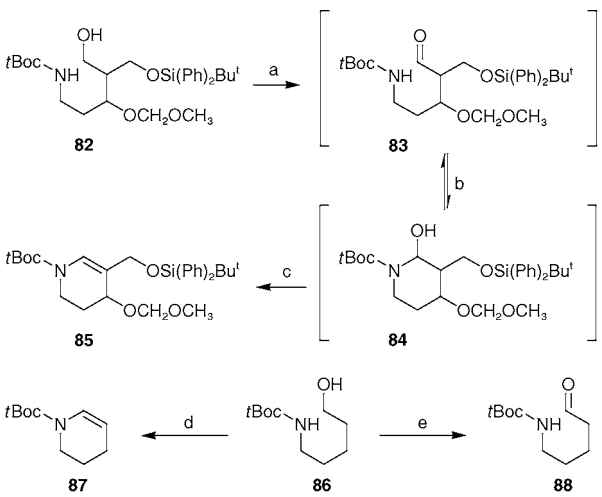
1,4-oxazines **94** or **96**, respectively (Scheme 18) [62].

Complex heterocycles are, thus, readily accessible in one pot from aryl amides, urethanes, and ureas.

Besides DMP its congener and precursor 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide (IBX) [63] has been used as an efficient oxidant for the cyclization of **97** or **99** to the 5-membered heterocycle **98** or **100**, respectively (Schemes 19 and 20) [64].

The scope, generality, and a rationale for the mechanism of these synthetically useful cyclizations in Schemes 18, 19, and 20 have been discussed.

Furthermore, Schemes 16 and 17 allow easy access to arrays of the target heterocycles **98** and **100**.



a. [O]. b. cyclization. c. dehydration. d. Dess-Martin, Periodinane, (92%).
e. Swern oxidation, (100%)

SCHEME 16

METAL-MEDIATED CYCLIZATION

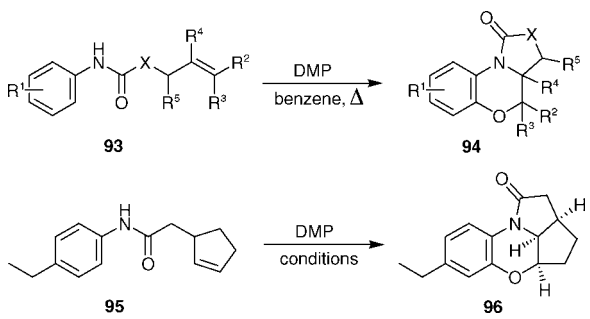
Metal-mediated reactions (cyclizations among them) have greatly contributed to the rapid growth of organic synthesis methodologies [6–18]. Useful synthetic methods and transformations have been and continue to be developed by means of metal species in catalytic or stoichiometric quantities.

Main Group Metal-Mediated Cyclization

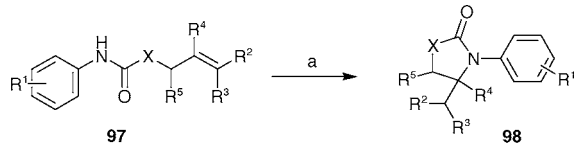
The reagents used are main group metal complexes in their higher valencies and they trigger cyclization by a ligand coupling process [34] (see introductory comments of the previous section).

The alcohol **106**, an intermediate in a reaction sequence aiming at the synthesis of oxygenated benzopyranquinones **101**, undergoes a $Hg(OAc)_2$-promoted cyclization to a diastereoisomeric mixture of **107** and **108** in high yield (Scheme 21) [65,66].

On the other hand, alcohol **110** undergoes a double-bond isomerization to **111**, followed by oxidative ring closure and subsequent reduction to **112** and **113** or **114** and **115** (Scheme 22).



SCHEME 18



97 **98**

a. IBX, THF:DMSO (10:1), 90 °C

SCHEME 19

Ag_2O oxidation of **113** or **114** and **115** gives a high yield of the targets **102** or **103**, respectively (Scheme 21).

Thallium(III) reagents have demonstrated unique oxidizing capacity in synthesis [67]. Thallium(III) nitrate (TTN) has been used to effect oxidative cyclization of various phenolic substrates via rearrangement [68]. It has been found that the reaction course is sensitive to the nature of substituents [69,70].

TTN-mediated cyclization of chalcones **116** leads to **117** or **118**, exemplifying the significance of substituent effects (Scheme 23) [71].

The first direct transformation of 2,2′-dihydroxychalcones into coumestans was reported [72]. Thus, treatment of **119** with TTN in methanol and subsequently with methanol/HCl in the presence of oxygen yields **120** (Scheme 24).

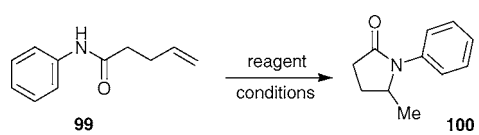
1,2,4-Triazole-fused quinolines have been obtained by Tl(III)-mediated oxidative cyclization of their quinoline hydrazones [73].

Lead(IV) acetate (LTA) has been one of the most commonly employed one-electron oxidants for a long time [74]. However, environmental concerns, nowadays, encourage its replacement by PIDA or PIFA as an equally effective, yet less toxic counterpart (see previous section).

LTA-promoted ring closure of alcohols **121** accompanied by carbonylation to δ-lactones **126** has been reported (Scheme 25) [75].

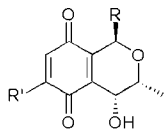
The postulated 1,5-hydrogen shift [76] is crucial to the feasibility of the cyclization. The reaction proved to be a general scheme for the synthesis of δ-lactones from saturated alcohols. It also demonstrates the potential of free-radical cyclization method.

Oxazolo[5,4-*b*]pyridines **131** have been prepared by the sequence shown in Scheme 26 [77]. The key step is the oxidative cyclization of the imine **130**.

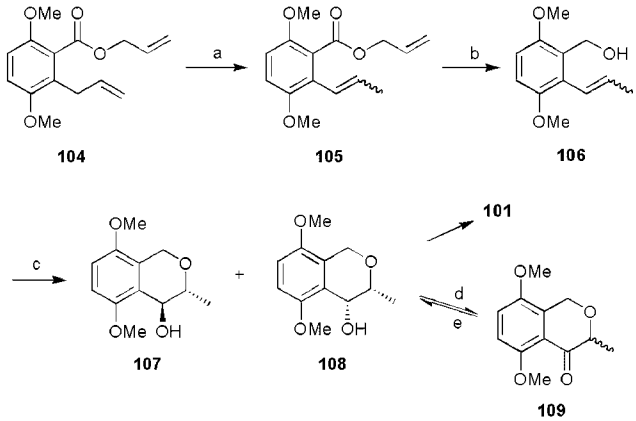


99 **100**

SCHEME 20



101 R'= R= H
102 R'= OMe; R= H
103 R'= OMe; R= Me

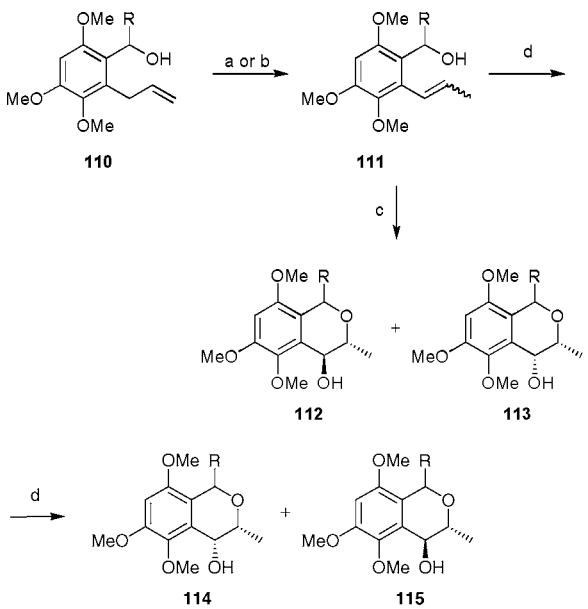


104 **105** **106** **107** **108** **109**

a. $KOBu^t$, DMF. b. LAH, Et_2O c. $Hg(OAc)_2$, O_2, $NaBH_4$, DMF.
d. PCC, CH_2Cl_2. e. LAH, Et_2O

SCHEME 21

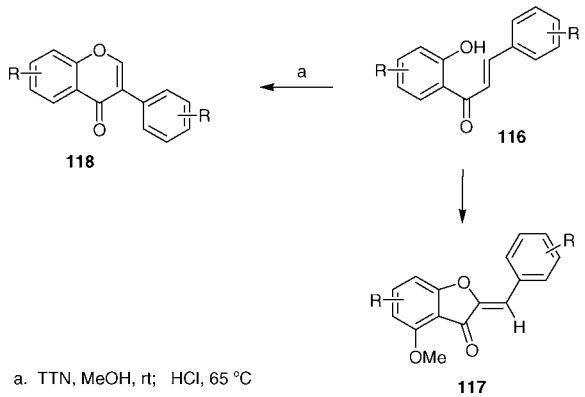
4-Hydroxy-2-cyclo-butenones, which are readily available from diethylsquarate, react with LTA to give 5-acetoxy-2(5*H*)-furanones **134** and 5-alkylidene-2(5*H*)-furanones **135** (Scheme 27) [78]. These



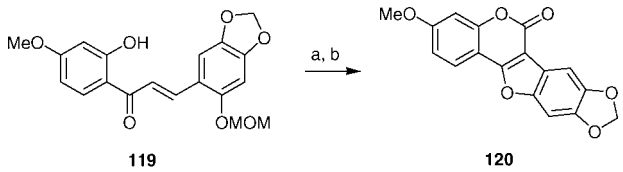
110 **111** **112** **113** **114** **115**

a. $KOBu^t$, DMF. b. $PdCl_2(MeCN)_2$, CH_2Cl_2. c. $Hg(OAc)_2$, O_2, $NaBH_4$, DMF.
d. $Hg(OAc)_2$, $NaBH_4$, DMF.

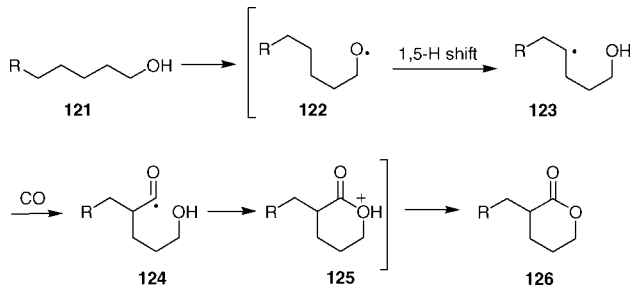
SCHEME 22



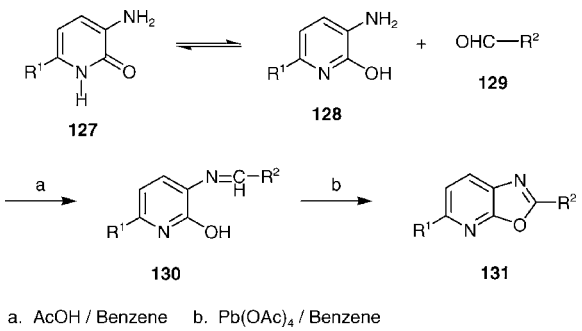
SCHEME 23



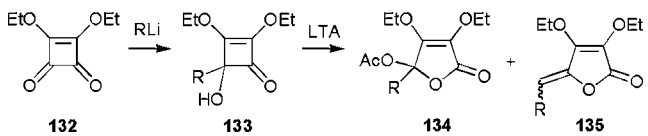
SCHEME 24



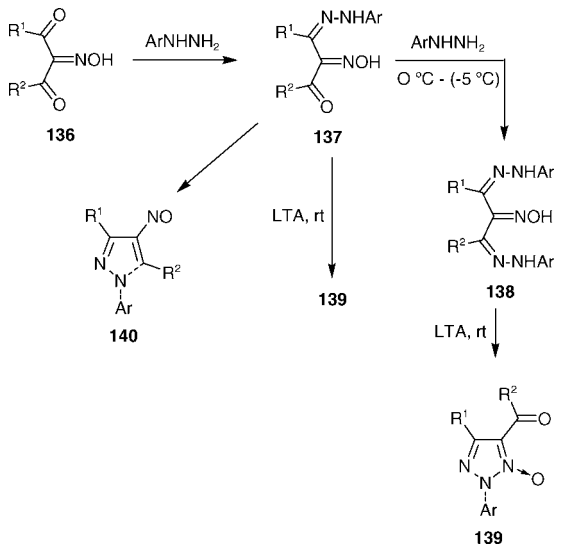
SCHEME 25



SCHEME 26



SCHEME 27



SCHEME 28

reactions extend the synthetic utility of squaric acid considerably.

The synthesis of 2,4,5-trisubstituted 1,2,3-triazole 1-oxides **139** has been reported by the LTA oxidative cyclization of oxime hydrazones **137** or **138** (Scheme 28) [79].

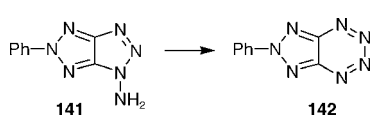
LTA-triggered oxidative rearrangement of *N*-amino triazoles **141** results in ring expansion to 1,2,3,4-tetrazines **142** (Scheme 29) [80,81].

The fusion of a triazole onto the *N*-amino triazole fragment deters the intermediacy of a hetaryne and thence any undesirable reactions, in accord with earlier reports [82].

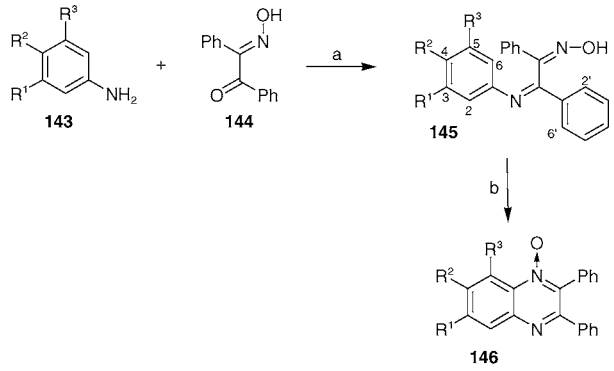
Oxime *N*-aryl imines **145** yield quinoxaline 1-oxides **146** upon LTA-mediated ring closure (Scheme 30) [83].

11*H*-dibenz[*b*,*e*]azepin-11-ones **149** have been prepared by LTA-mediated oxidative cyclization rearrangement of *N*-aryl-hydrazones **148** (Scheme 31) [84].

LTA-triggered *o*- and/or *peri*-substituent-dependent cyclization of 2-hydroxy-1-acyl naphthalene oximes **150** gives rise to 1,2-oxazole 2-oxides **151**, 1,2-oxazines **154**, and *N*-hydroxy-indoles **155** (Scheme 32) [85,86]. PIDA and PIFA have proved to be equally effective (P. G. Tsoungas, unpublished results).



SCHEME 29



a. EtOH/H_2O, Reflux, 28 - 75%. b. $(AcO)_4Pb/CH_2Cl_2$, r.t., 27 - 71%.

SCHEME 30

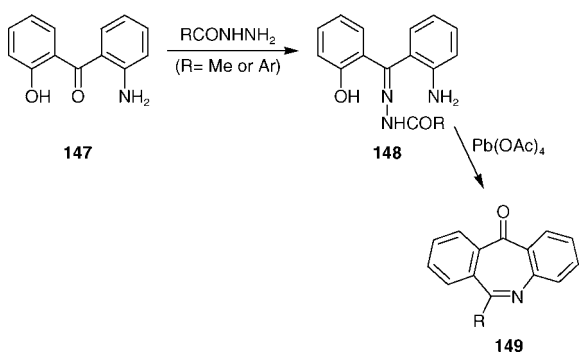
Oxidative cyclization of amides **156** to triazoles **158** and subsequently to **159** has been accomplished by either LTA or PIDA (Scheme 33) [87].

Transition-Metal-Mediated Cyclization

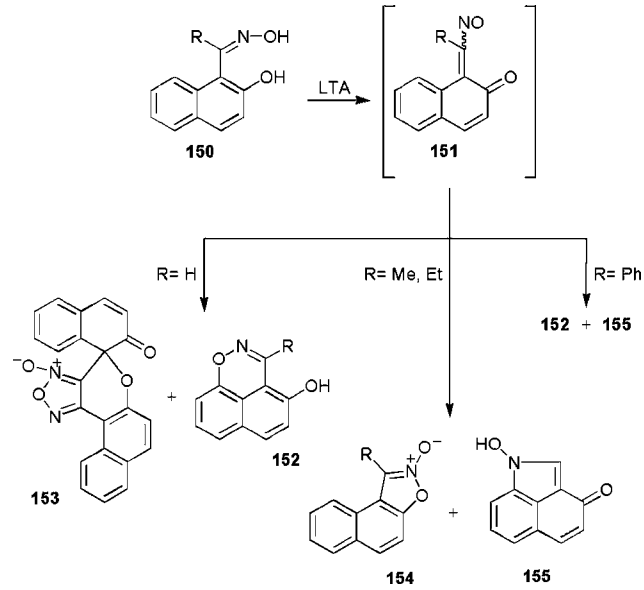
Transition-metal complexes have proved to be invaluable reagents to a dearth of synthetic transformations [8–18]. The latter provide access to complex frameworks efficiently and selectively from readily available substrates. It is beyond doubt that a major part of today's astonishing achievements in organic synthesis is attributed to them.

Pd-mediated C—X (X = N, O) bond formation has been recorded as a particularly useful method in organic synthesis [88]. Its intramolecular variant has been extensively used to construct 5- and 6-membered heterocyclic structures.

A variety of *O*-containing heterocycles have been prepared by Pd(II)-induced cyclization of hydroxy-bearing alkenes, dienes, and alkynes [89]. Intramolecular oxypalladation is the key step of this overall oxidative cyclization process.



SCHEME 31



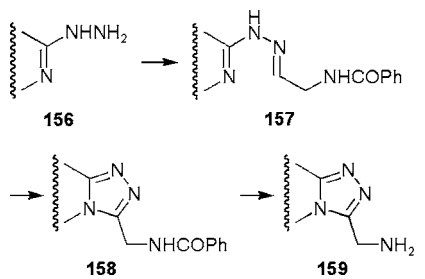
SCHEME 32

Various carbazole-containing polycyclic structures have been assembled by Pd(II)-mediated C—C oxidative coupling of a diaryl amine **160** to the carbazole segment **161** of the framework (Scheme 34).

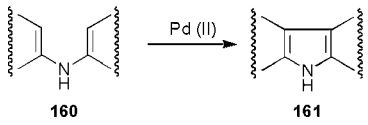
Accordingly, pyrido[4,3,*b*]carbazoles [90], intermediates to ellipticines and olivacines, kinamycins, and analogues [91–93], as well as multisubstituted carbazoloquinones [94] have been obtained. In some cases the oxidative coupling has been effected by a mixture of Pd(II) and Cu(II) complexes.

Pd(II)-catalyzed 1,4-oxidation of 1,3-dienes is a very important transformation in organic synthesis, partly because of its high regio- and stereoselectivity [95–97]. Its intramolecular variant has emerged as an efficient method for the stereoselective synthesis of various heterocycles through cyclization modes (I)–(III) (Scheme 35) [95,98].

Stereo-controlled Pd(II)-mediated cyclization of diene alcohols **168** or **170** to tetrahydrofurans (THF) **169** or tetrahydropyrans (THP) **171** has been reported (Scheme 36) [98].



SCHEME 33



SCHEME 34

Diene alcohols **172** are cyclized to THF spiro derivatives **174** with cis stereochemistry [99]. The stereochemical outcome has been rationalized by invoking an intramolecular trans-alkoxypalladation of alcohol **172** to a π-allyl intermediate **173**, followed by an external trans-attack of solvent alcohol leading to **174** (Scheme 37).

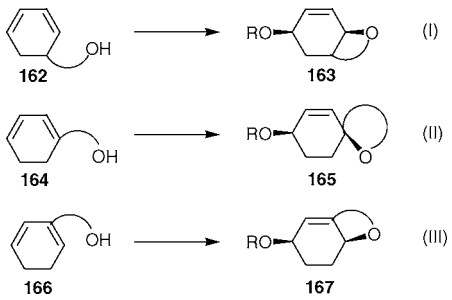
On the other hand, alcohols **175** or **177** lead to pyrans **176** or **178** stereoselectively (Scheme 38) [99].

Pd(II)-mediated asymmetric oxidations have received scant attention. There have been only a few early reports on catalytic asymmetric Wacker-type intramolecular Pd(II)-catalyzed oxidative cyclization of *o*-allylphenols to dihydrobenzofurans [100]. A similar cyclization with a high enantioselectivity (>97% ee) has been reported recently (Scheme 39) [101]. The Pd(II) catalyst used is coordinated with chiral bis(oxazoline) ligands based on 1,1′-binaphthyl backbone.

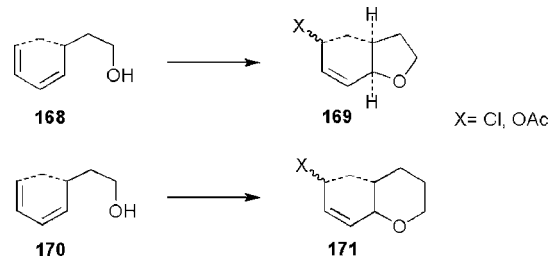
Pd(II)-catalyzed oxidative coupling of phenols **183** with alkenes **184** gives rise to dibenzo[*b*,*d*]pyrans **185** (Scheme 40) [102].

The cyclization is considered to be a case of functional-group-assisted catalytic oxidation of an aromatic C—H bond with reasonable efficiency [103,104].

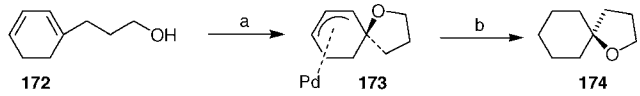
A new catalyst system has been developed for the Pd-catalyzed cyclization of olefinic tosylamides [105]. Whereas typical conditions require either stoichiometric amounts of Pd(II) salts or catalytic amounts of Pd(II) in the presence of benzoquinone as a reoxidant, the new catalyst system utilizes catalytic $Pd(OAc)_2$ under an atmosphere of O_2 in DMSO with no additional reoxidant. Although *o*-vinylic



SCHEME 35

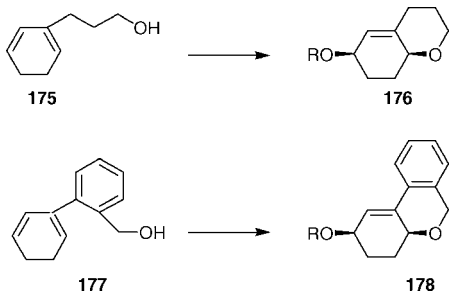


SCHEME 36

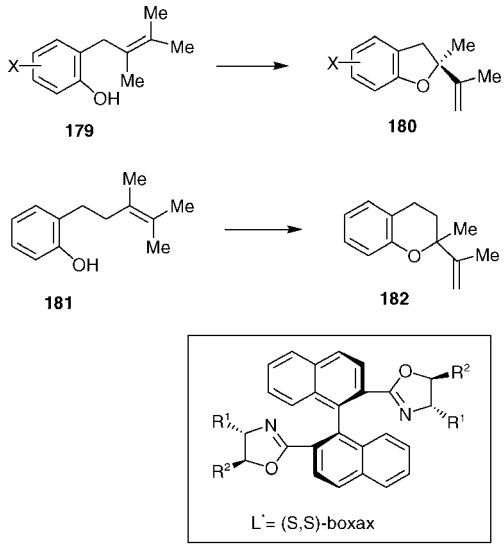


a. $Pd(OAc)_2$, $MeSO_3H$(cat.), benzoquinone / MeOH. b. MeOH

SCHEME 37

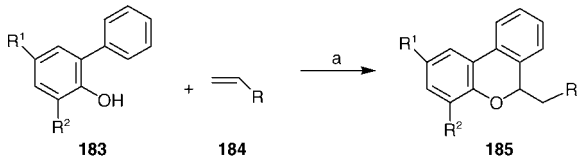


SCHEME 38



a. Pd(II)-L*, L*. b. Pd(II)-L*, (S,S)-bn-boxax

SCHEME 39



a. Pd $(OAc)_2$, $Cu(OAc)_2.H_20$, MS 4A, air

SCHEME 40

tosylamides **186** can be cyclized to *N*-tosylindoles **187** using this catalyst system, $PdCl_2$/benzoquinone is more effective for such cyclizations (Scheme 41).

A convergent synthesis of the aglycone of *gilvocarsins M* and *E* **189** engages a Pd-catalyzed intramolecular coupling as the key step [106]. The reaction is based on the "lactone concept" (Scheme 42) [107].

Similarly naphthylisoquinoline alkaloid dioncophylline *P*-4 and its atropo-diastereomer *M*-4 have been prepared using the "lactone" methodology (Scheme 43) [108].

o-Alkenylbenzyl alcohols **195** or their 2-allyl-3-hydroxyalkyl analogues **197** are Pd(II)-cyclized to isochromenes **196** and **198** or their benzoisochromequinone derivatives (Scheme 44) [109].

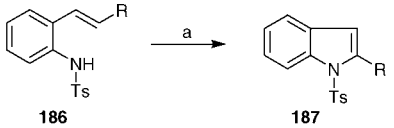
The intramolecular coupling of ethers **199** under basic conditions shows good ortho-selectivity and leads to high yields of dibenzo[*b*,*d*]pyrans **200** when catalyzed by $Pd(PPh_3)_4$. 2-Phenylphenols undergo a Pd–Cu-catalyzed oxidative coupling with alkenes to give this dibenzopyran (Scheme 45) [110].

Other interesting Pd(II)-induced dehydrohalogenative intramolecular couplings resulting in an overall oxidative cyclization to a variety of *N*,*O*-heterocycles have been reported [111].

N-Arylation of 3-aminoquinoline **201** with $Ph_3Bi(OAc)_2$ followed by Pd(II)-mediated oxidative cyclization serves as an efficient route to indolo[3,2-*b*]quinolines **202** (Scheme 46) [112].

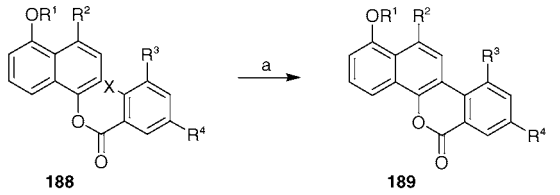
Manganese(III)-mediated oxidative free-radical cyclizations have been extensively studied and the field has been elegantly covered [113].

While Mn(III) or Mn(III)/Cu(II) have been used for the major part of the work, other one-electron



a. Pd $(OAc)_2$ (5 mol %), DMSO, O_2 (1 atm), NaOAc (2 equiv)

SCHEME 41



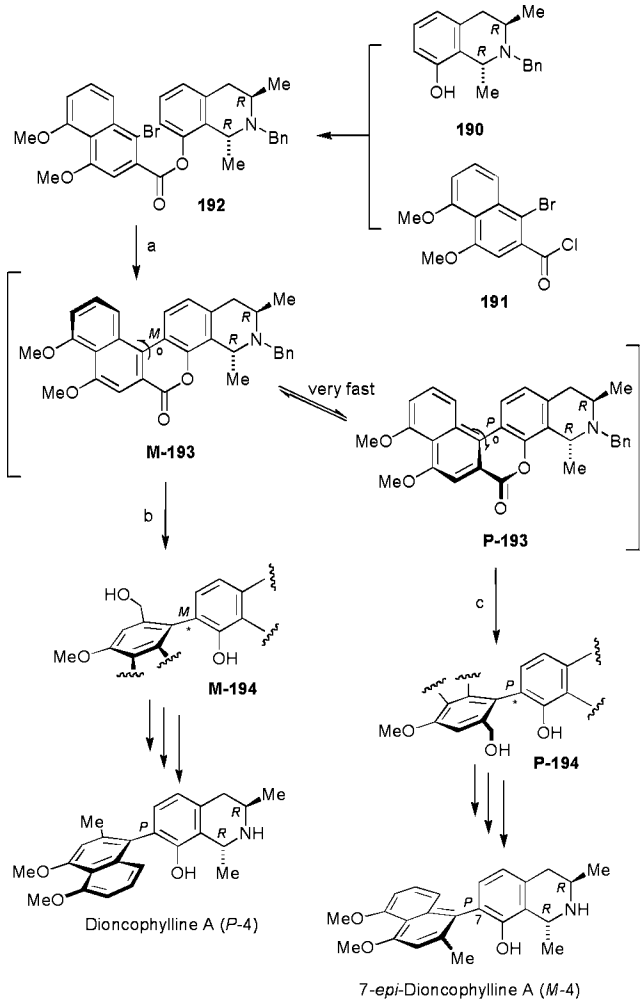
a. $Pd(PPh_3)_2Cl_2$, NaOAc / DMA, 130 °C 2-3h

R^1= Bn
R^2= R^3= OMe
R^4= CH_2R
X= Br, I

SCHEME 42

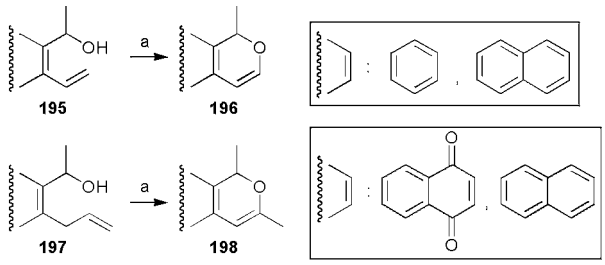
oxidants, notably Ce(IV), Fe(III), and Cu(II) have also been employed (see later).

Commercially available $Mn(OAc)_3 \cdot 2H_2O$ is the reagent for the oxidative cyclizations. The anhydrous form is more reactive and reaction times somewhat shorter, but yields in both cases are comparable.



a. Pd^{II}, b. $AlMe_3$ / "RedAl", dr > 95:5. c. dr 87:13, "RedAl"

SCHEME 43



a. $PdCl_2(CH_3CN)_2$, CH_2Cl_2, r.t.

SCHEME 44

Some Mn(III)- or Mn(II)-induced cyclizations are discussed. Mn(III)-initiated radical reaction of nitroacetate **204** to 1,4-naphoquinone **203** results in overall oxidative cyclodehydration to fused isoxazoles **205** (Scheme 47) [114].

Unsaturated nitroacetates **208**, when oxidatively cyclized by $Mn(OAc)_3$ to **207**, provide a facile route to these amino acid precursors (Scheme 48) [115].

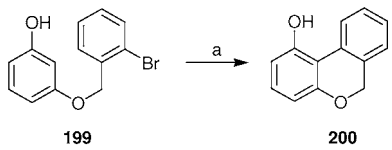
The reaction of **208** with Mn(III) species should generate enolate **209**. The latter is transformed to radical **210**, which upon oxidative cyclization gives **212**. No isoxazoline *N*-oxide **211** is formed. An alternative dehydrative decomposition of **209** leads to nitrile oxide **213**, which undergoes intramolecular 1,3-dipolar cycloaddition to **214** (Scheme 49).

Fe(III)-activated diene complexes **215** have been oxidatively cyclized to carbazole antibiotics carbazomycins **216** with very active MnO_2 (Scheme 50) [116].

Using this oxidative coupling methodology carbazomycin analogues have been reported [117]. Deuterium labeling studies provided unequivocal determination of the regioselectivity and stereospecificity of the cyclization reaction [118].

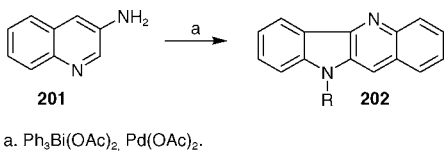
N-Acylenamines **217** react with $Mn(OAc)_3$ to form functionalized pyrrolidines **218** via a disfavored 5-*endo-trig* radical cyclization (Scheme 51) [119].

1,2,3-Triazole *N*-oxides have been prepared by MnO_2 oxidative cyclization of their corresponding hydrazone precursors [120].



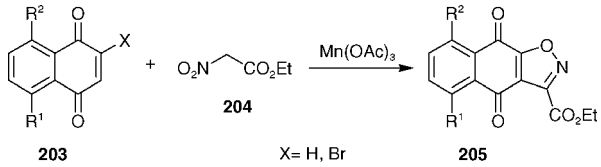
a. $Pd(PPh_3)_4$, ^tBuOK, DMA. 95 °C

SCHEME 45

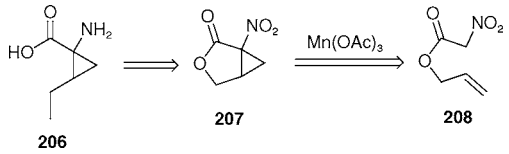


a. $Ph_3Bi(OAc)_2$, $Pd(OAc)_2$.

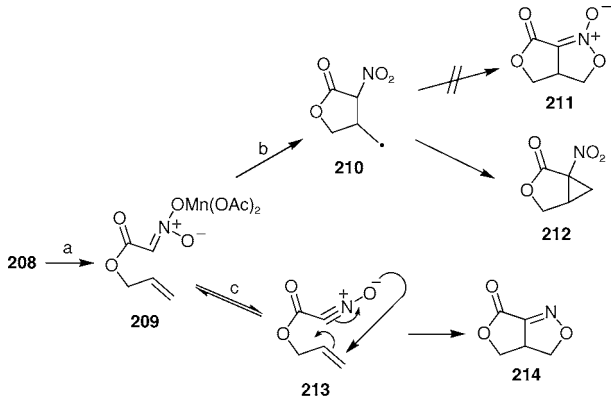
SCHEME 46



SCHEME 47

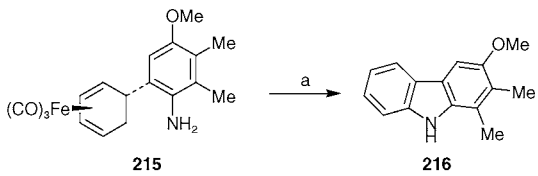


SCHEME 48



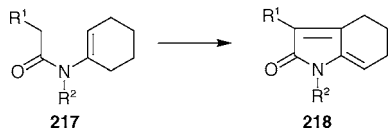
a. Mn(III) / $Cu(OAc)_2$, HOAc, Δ. b. - $Mn(OAc)_2$. c. $Mn(OAc)_2OH$

SCHEME 49

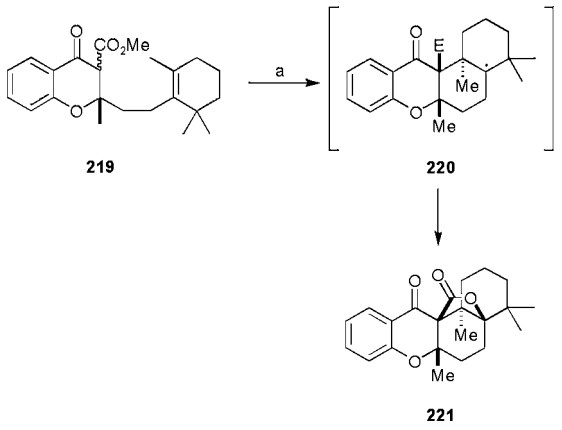


a. MnO_2, toluene, r.t.

SCHEME 50



SCHEME 51



a. $Mn(OAc)_3$, $Cu(OAc)_2$, HOAc, 58 °C, 5h, 25%

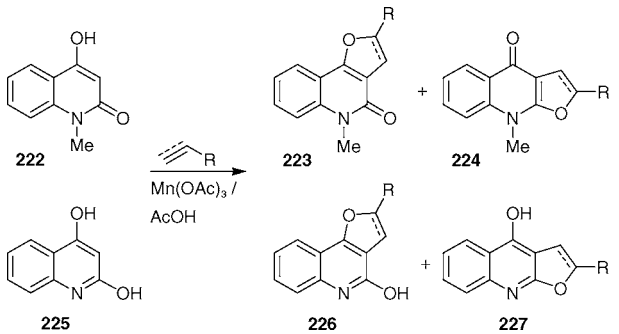
SCHEME 52

The manganese(III) acetate mediated oxidative cyclization of β-ketoesters has been utilized to construct a pentacyclic compound in low yield [121]. The intermediate radical **220** formed from an initial 6-*endo-trig* reaction undergoes further lactonization in the presence of copper(II) acetate. The compound **221** has the basic skeleton found in fungal metabolite sesquiterpene phenols (Scheme 52).

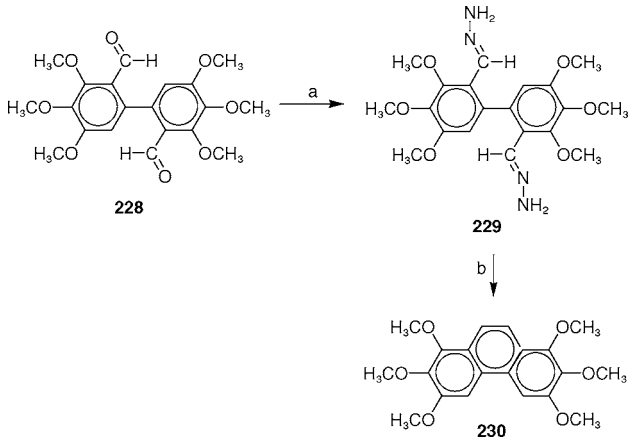
Mn(III)-mediated radical cyclization of quinolines **222** or **225** to tricyclic quinoline alkaloids **223** or **226**, respectively, has been achieved (Scheme 53) [122].

Both angular **223** (**226**) and linear **224** (**227**) structures are formed, the regioselectivity of the cyclization and hence product distribution being dependent on the nature of substituent(s) on the alkene (alkyne). Furthermore, the efficiency of the reaction has been found to depend on the mole ratio of reactants and the presence of a co-oxidant ($KMnO_4$ has been very effective).

Cu(I)-promoted oxidative cyclization of bishydrazones **229** to phenanthrenes **230** in high yields has been effected (Scheme 54) [123].



SCHEME 53



a. N_2H_4, H_2O, *i*PrOH. b. CuCl / O_2 / C_5H_5N.

SCHEME 54

A Cu(II)-mediated competition between oxidative coupling-cyclization and oxidative coupling-dimerization has been described with 2-aminonaphthalenes **231, 232, 237**, and **238** (Scheme 55) [124].

Fused quinoxalines **243** and **245** have been obtained by Cu(II)-mediated oxidative cyclization of azo compounds **242** and **244** (Scheme 56) [125].

The method has also been applied to the synthesis of fused 1,2,3-triazoles **247** from their azo precursors **246** (Scheme 57) [126].

A versatile Cu(II)-triggered oxidative cyclization scheme leading to substituted pyrazole 1-oxides **250, 253, 255, 258, 260**, and **263**, has been described (Scheme 58) [127].

Oxidation of the oximes, either as *E*/*Z* mixtures or their individual constituent isomers, revealed that the *E*-isomer reacts faster.

1,2,3-Triazoles have also been obtained from a Cu(II)-mediated oxidative cyclization of O-protected oximes **266–268** (Scheme 59) [128].

$CuSO_4$ proved to be most effective but MnO_2 and NiO_2 also served well as one-electron oxidants.

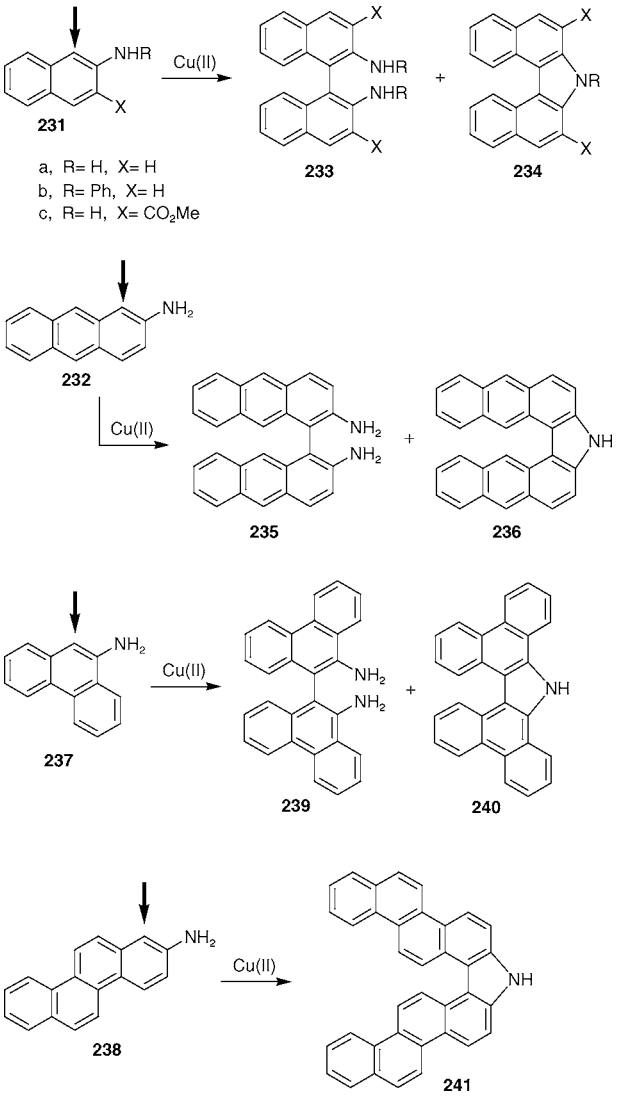
Polycyclic quinones **272** and **273** have been obtained by $CuO–K_2CO_3$-catalyzed cyclization of **270** and **271** respectively (Scheme 60) [129].

Co(IV)-mediated cyclization of alkenyl aryl ethers **274** leads to benzopyrans **275** and **276** in a 1:1 ratio (Scheme 61) [130].

Co(I) reagents have been used to effect radical oxidative cyclizations of alkyl and aryl halides to heterocycles and γ-lactones [131].

A Cr–Mn redox couple has been ingeniously used to trigger a domino process (Scheme 62) [132].

The reagent initially catalyzes the reduction of *o*-hydroxy nitroarene **277** and then effects the oxidative cyclization of the imine **280**.



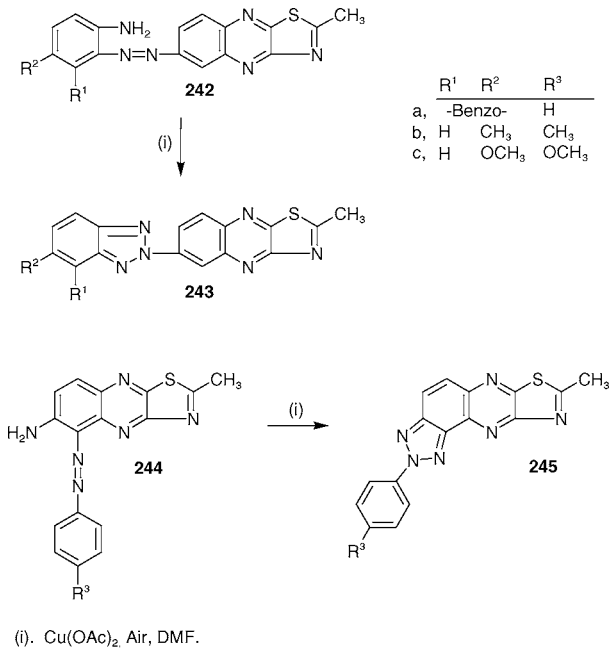
SCHEME 55

A broad range of substituted 4a,9a-dihydro-9*H*-carbazoles **216** have been prepared by Fe-mediated cyclization of suitably activated organo-iron amine complexes **215** (see Scheme 50). Interestingly, oxidative cyclization without subsequent aromatization could be achieved by SET oxidants such as ferricenium hexafluorophosphate (see also Schemes 34 and 35) [133].

Amidrazines **283** or **285** have been cyclized to triazoles **284** and **286** by Fe(III) oxidation (Scheme 63) [134].

NiO_2 and LTA have also been used but with results inferior to those of $FeCl_3$.

Iron complexes are known to trigger an oxidative cyclization of ω-enedienes through a π-allyl complex. There exist only a few examples on carbocyclization and none on heterocyclizations [135].



SCHEME 56

Substituted 1,3,4-oxadiazoles have been obtained by $FeCl_3$-induced oxidative cyclization of their corresponding hydrazones [136].

Amino alcohols **287** undergo a Ru-promoted oxidative ring closure to lactams **288** (Scheme 64) [137].

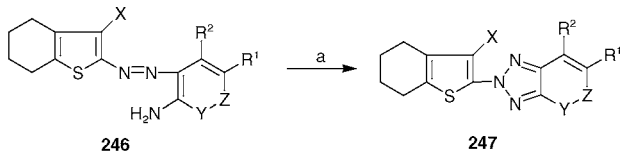
The following rationale has been proposed for the conversion (Scheme 65).

The concept has been extended to a synthetically useful condensation of aldehydes and amines to amides [138].

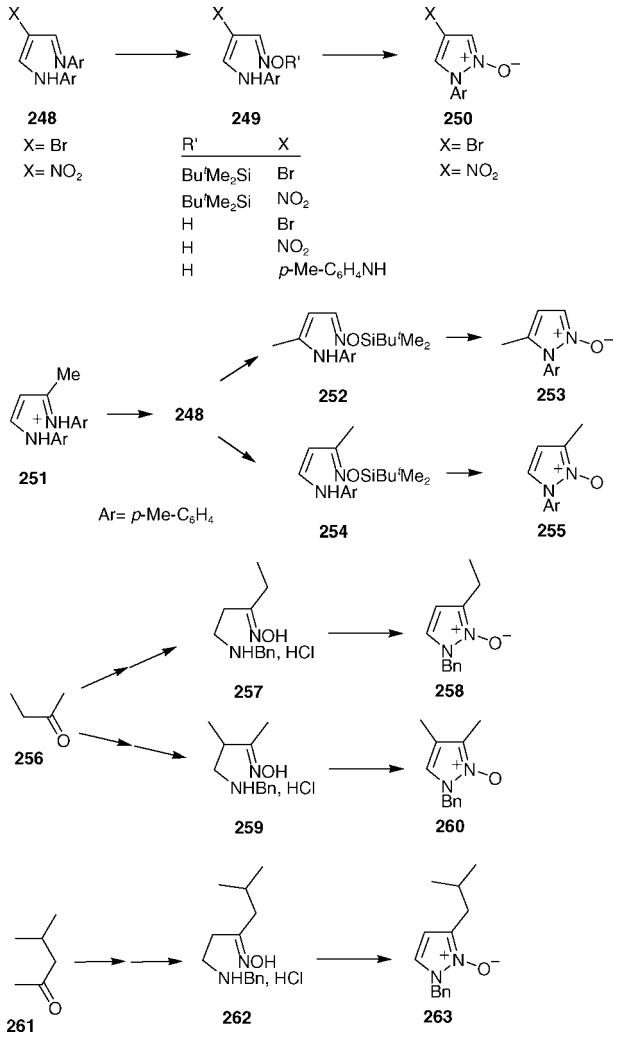
By analogy 1,4- and 1,5-diols **293** and **295** are oxidatively cyclized to γ-lactones **294** and 1,4-oxazin-2-ones **296** respectively (Scheme 66) [138].

Acetone [138], diphenylacetylene [139,140], and benzylidenacetone [138] have been used as effective hydrogen acceptors, acetone being the most convenient one.

Arylnaphthalene ligands such as retronecine **298**, justicidine A **299** [141], and L-lyxose derivatives **301** [142] have been obtained using the cyclization approach (Scheme 67).



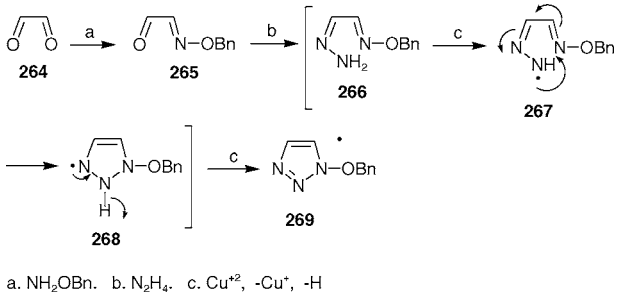
SCHEME 57



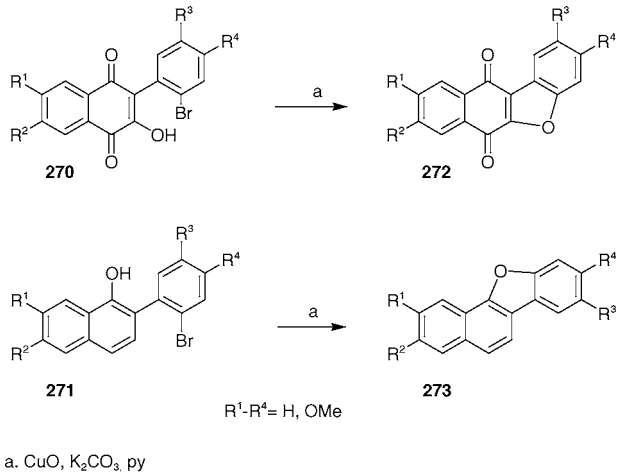
SCHEME 58

Asymmetric lactonization of prochiral diols has been achieved with chiral phosphine complex catalysts (Scheme 68) [143].

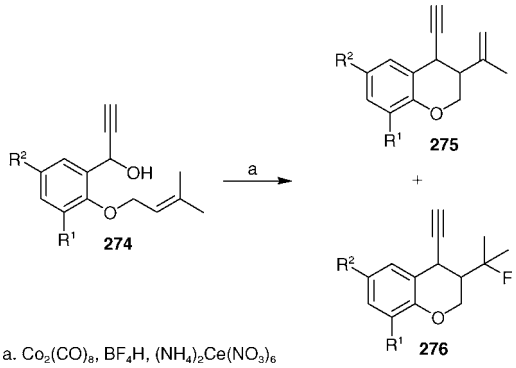
Ru oxides are widely used powerful oxidants [144]. In combination with Lewis acids RuO_2 has been effectively employed in intramolecular



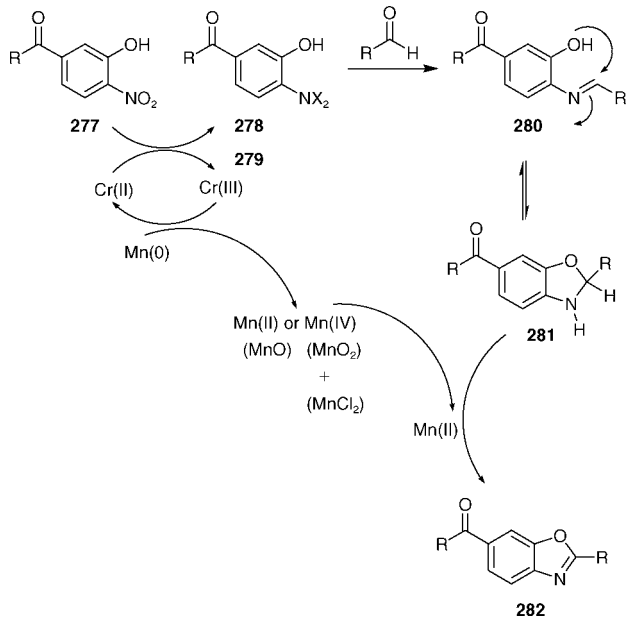
SCHEME 59



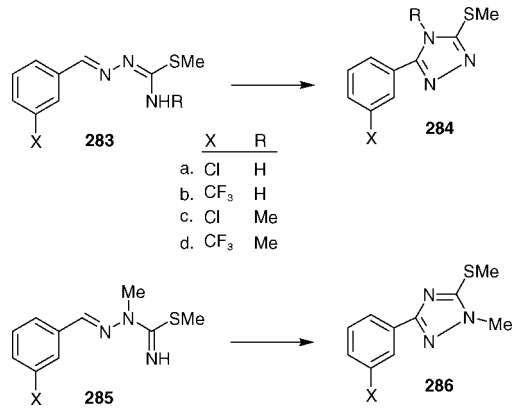
SCHEME 60



SCHEME 61



SCHEME 62



SCHEME 63

oxidative coupling of phenols [145] and aromatic rings [146] bearing electron-donating substituents.

A Ru-mediated modification of Friedlaender quinoline synthesis has been reported (Scheme 69) [147].

An array of Ru catalysts of diverse reactivities has been tested to optimize reaction conditions.

1,5-Dienes **306, 308**, and **310** are oxidatively cyclized to THF diols **307, 309, 311**, and **312** by a RuO_4-catalyzed reaction (Scheme 70) [148].

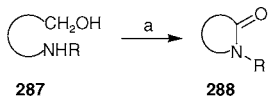
Alkenic steroids have also been treated with the reagent to give 1,2-diols [149]. A similar approach has recently been adopted for the Ru(III)-mediated cyclization of 1,6-dienes to stereoselectively prepared disubstituted tetrahydropyran-diols [150].

Oxidative cyclization of derivatives of *o*-aminophenylethanol, which has previously been applied to simple indoles, was used with more elaborate structures in the preparation of teleocidin analogues (Scheme 71) [151].

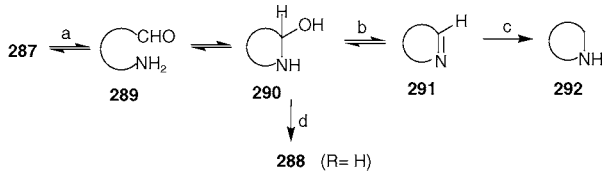
The use of Ru complexes as catalysts in organic synthesis has been perceptively reviewed recently [144].

A tandem polycyclization of polyenic alcohols **315** into poly-THF products **319–322**, triggered by Re(VII) reagents, is a useful methodology of high diastereoselectivity for the synthesis of these molecules (Scheme 72) [152].

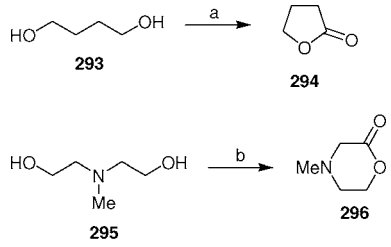
Spirocyclization of oximes **323** by Bu_4NReO_4 gives rise to azaspirodienones **324**. The latter are easily transformed to quinolines via dienonephenol rearrangement (Scheme 73) [153].



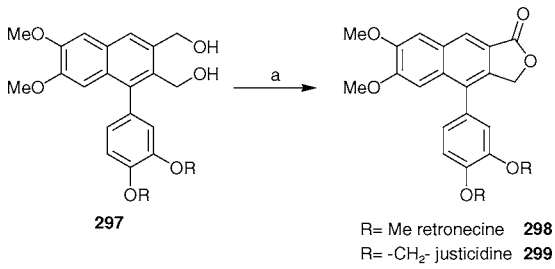
SCHEME 64

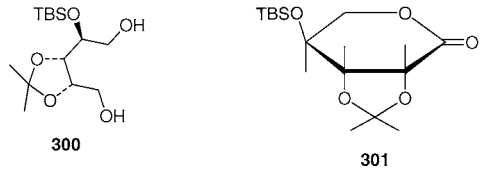


SCHEME 65

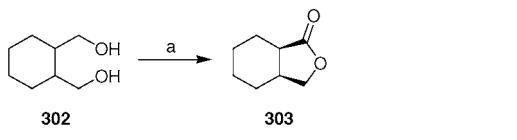


SCHEME 66

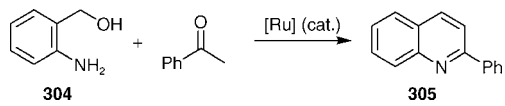




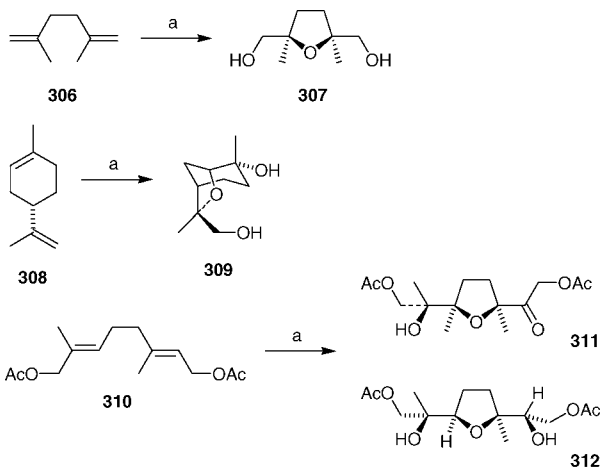
SCHEME 67



SCHEME 68

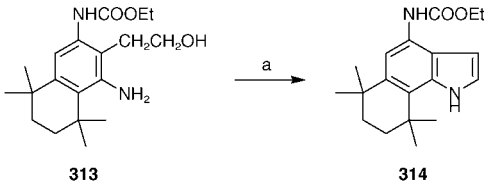


SCHEME 69



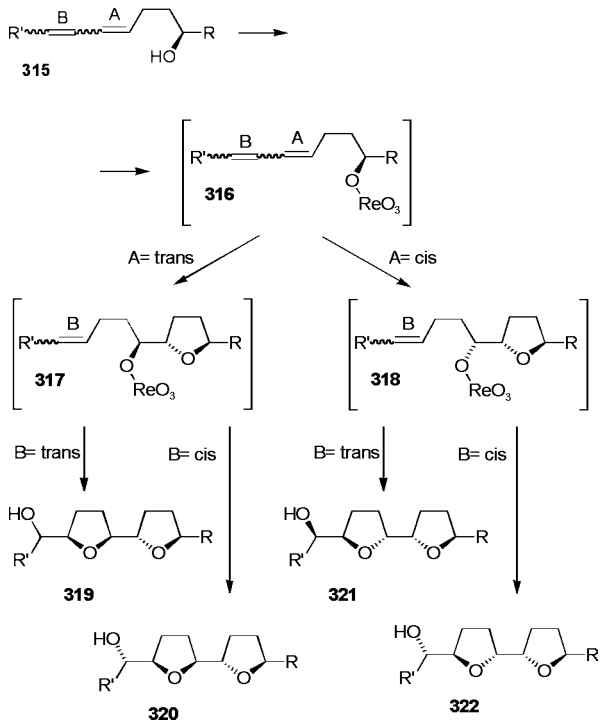
a. $RuO_4.2H_2O$, $NaIO_4$, EtOAc / acetone / H_2O (2:1:1, v/v)

SCHEME 70

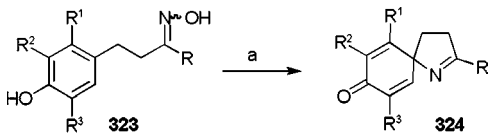


a. $Ru(PPh_3)_2Cl_2$

SCHEME 71



SCHEME 72



a. Bu_4NReO_4, CF_3SO_3H, $ClCH_2CH_2Cl$, reflux

SCHEME 73

OsO_4/TMEDA has been found to be an effective oxidant for cyclic allylic alcohols [154] and amides [155]. The reagent has also been successfully applied in the oxidative cyclization of 1,5-dienes **325–328** to functionalized THFs **329–332** with high stereoselectivity (Scheme 74) [156–158].

1,4-Dienes have also been cyclized to trisubstituted THF-diols by OsO_4 [159].

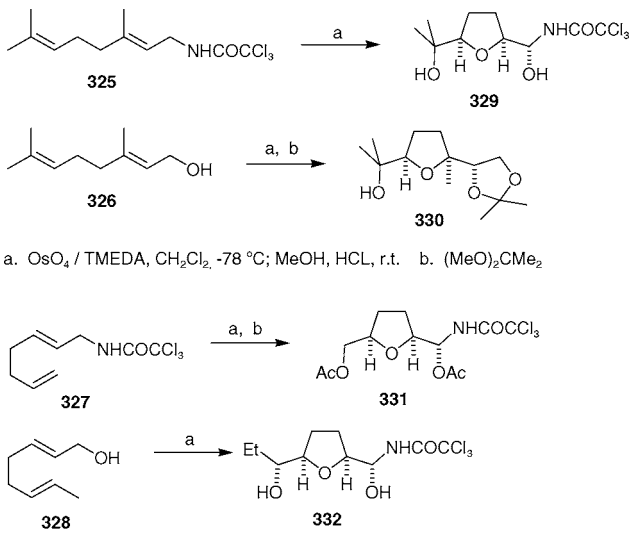
In a reaction sequence targeted on pyranonaphthoquinones **336** and **337** the key step is the OsO_4/$NaIO_4$ (Lemieux—Johnson)-mediated oxidative 6-*exo-trig* cyclization of **334** to pyran **335** (Scheme 75) [160].

An improved synthesis of 1,3,5-trisubstituted 1,2,4-triazoles **339** has been accomplished by a Ag_2CO_3-mediated oxidative cyclization of amidrazines **338** (Scheme 76) [161].

The approach is flexible and compatible with a broad range of functional groups.

Lanthanide-Mediated Cyclization

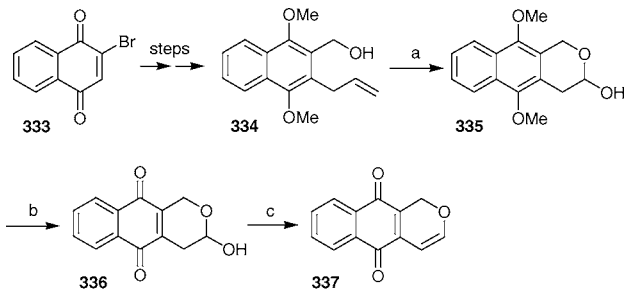
The applications of lanthanide reagents in organic synthesis have been elegantly reviewed some time ago [162].



a. OsO_4 / TMEDA, CH_2Cl_2, -78 °C; MeOH, HCL, r.t. b. $(MeO)_2CMe_2$

a. OsO_4 / TMEDA, CH_2Cl_2, -78 °C; MeOH, HCL, r.t. b. Ac_2O, Et_3N, CH_2Cl_2

SCHEME 74



a. OsO_4 (cat.), $NaIO_4$ (2.0 equiv.), dioxane / H_2O (3:1), r.t. b. CAN (3 equiv.), MeCN, H_2O, r.t. c. TsOH (cat.), benzene, Δ.

SCHEME 75

Ceric ammonium nitrate (CAN) is the best known and most widely used oxidant of lanthanide reagents [163]. Early oxidations with CAN had been carried out in strongly acidic media using stoichiometric quantities of the reagent. Later work has focused on milder and more convenient procedures.

Ce(IV) reagents are commonly employed in oxidative coupling reactions and many publications have alluded to the superiority of this oxidant over the more frequently used $Mn(OAc)_3$.

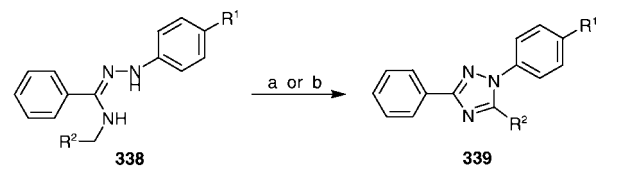
Oxidative cyclization of unsaturated silyl enol ethers **340** with CAN provides a stereoselective route to tricyclic ketones **341** (Scheme 77) [164].

Intramolecular CAN-promoted radical carbocyclization of α-substituted β-allyloxy nitro compounds **342** leads to functionalized THFs **344** and **345** (Scheme 78) [165].

CAN-oxidation of a heptenyl nitronate induces further oxidation to a [4.3.0]bicyclic heterocycle [166]. The THP structure is a key unit of various intermediates involved in the synthesis of polyethers and ionophore natural products [167]. Many methods have, thus, been developed for the stereoselective construction of the THP skeleton via C—C [168,169] and C—O [170] bond-forming reactions.

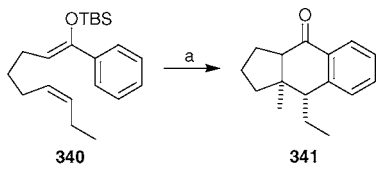
Recently, approaches to this target, such as **351**, have made use of nitroalkenes **346** through the reaction sequence shown (Scheme 79) [171].

Along similar lines, CAN-mediated oxidative cyclization of cinnamyl ethers **352** and **354** gives



a. H_2O_2 (30%) / KOH (90:10, v/v), CH_3CN, 0 °C to r.t. b. Ag_2CO_3, CH_3CN, 2h

SCHEME 76



a. CAN, $NaHCO_3$, MeCN, r.t.

SCHEME 77

rise to 3,4-trans-disubstituted THF derivatives **353** and **355**, respectively, with a high stereospecificity (Scheme 80) [172].

MISCELLANEOUS OXIDANT-MEDIATED CYCLIZATION

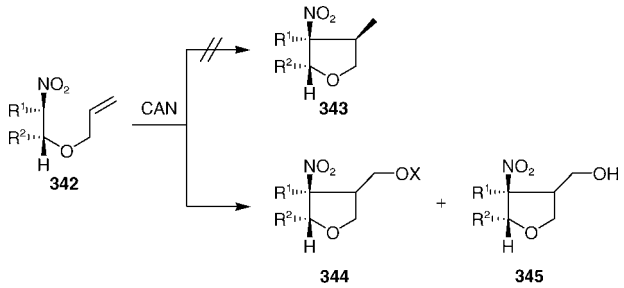
A salicylaldehyde-based [173], clay-catalyzed, expeditious synthesis of 1,3-benzoxazin-2-ones **360** by MW irradiation has been reported (Scheme 81) [177].

The overall oxidative cyclization of **356** by cyclodehydrazination to **360** is a facile route to this class of heterocycles [178–182]. A MW-mediated overall oxidation–cyclodehydration of 2-acylamino ketones **361** to oxazoles **362** has been effected (Scheme 82) [183]. A high yield route to 2,5-disubstituted oxazole-4-carboxylates has been reported using the methodology in reverse order [184].

Sodium perborate (SPB) and Sodium percarbonate (SPC) are known effective oxidants to a broad range of functional groups or transformations [185].

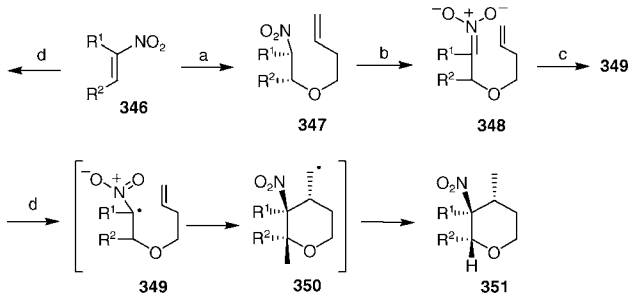
High yield oxidative cyclization of 2,5-diamino-1,4-benzoquinones **363** to linear pentacyclic bisoxazines **364** has been reported using either of the oxidants in concentrated sulfuric acid (Scheme 83) [186].

Benzopyranopyrazoles **366** have been obtained by the SeO_2-promoted oxidative cyclization of arylidenepyrazoles **365** (Scheme 84) [187].



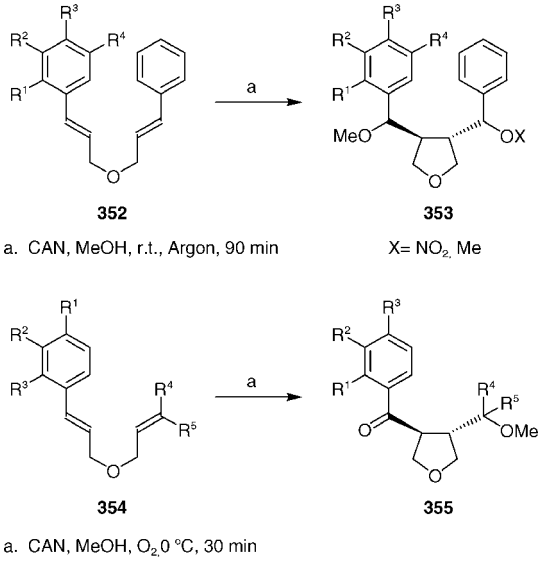
X= NO_2, H

SCHEME 78



a. Bu^{t}OK, BuOH, PhH; buten-3-ol, H$^+$. b. NaH, THF. c. CAN, THF, -78°C, d. NaH, THF; buten-3-ol; CAN, THF, -78°C; 0,1N $Na_2S_2O_3$

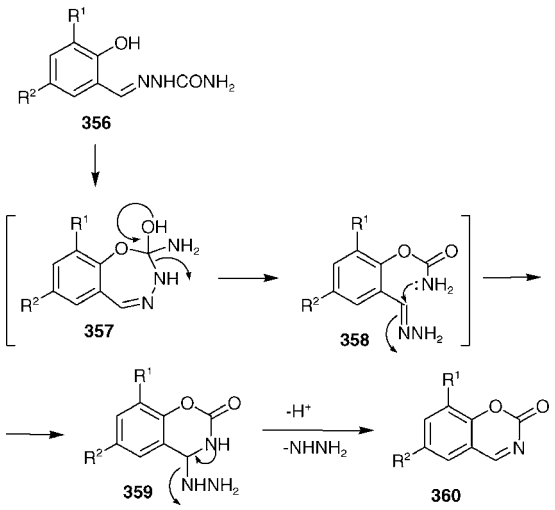
SCHEME 79



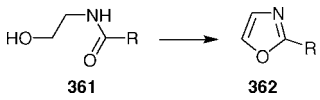
a. CAN, MeOH, r.t., Argon, 90 min X= NO_2, Me

a. CAN, MeOH, O_2, 0 °C, 30 min

SCHEME 80



SCHEME 81



SCHEME 82

Condensed quinoxalines with fluorescence properties have been prepared by an air-induced oxidative cyclization of their corresponding triazene precursors [188].

Carbazoles **216** (see Schemes 34, 50, and 55) have been prepared by air-triggered cyclization of amines **215** [189]. Air-mediated oxidative cyclization has also been used as the key step to make up the carbazole unit en route to the total synthesis of ±-carquinostatin A, a potent neuronal cell-protecting substance [189].

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) is a well-known and widely used oxidant [190]. Morpholine diones **368** and **370** have been prepared by a DDQ-promoted oxidative cyclization of amides **367** and **369** (Scheme 85) [191].

Nitrovinyl oximes **371** undergo oxidative cyclization to isoxazoles **372** by the action of DDQ or iodine/potassium iodide (Scheme 86) [192].

Solid-support synthesis of 5-substituted oxazoles **374** has been accomplished by DDQ-mediated oxidative cyclization of immobilized dipeptides **373** (Scheme 87) [193].

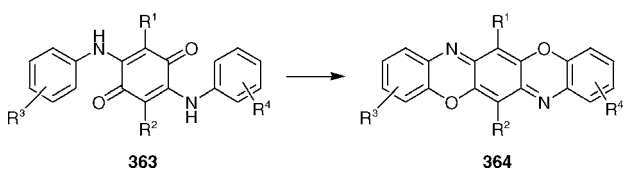
No reaction has been observed with other oxidants such as chloranil, CAN, or iodine. Alternatively, a solid-phase synthesis of **380** is described (Scheme 88) [193].

I_2/KI in alkaline solution effects the oxidative cyclization of substituted semicarbazides to 1,3,4-oxadiazoles [194]. I_2 has been used for the intramolecular trapping of benzynes **382** by a suitably situated phenol group (Scheme 89) [195].

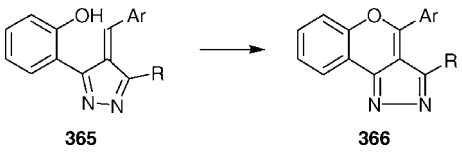
Oxadiazine derivatives **385** have been obtained by the $NaIO_4$-triggered oxidative cyclization of their precursor hydrazones **384** (Scheme 90) [196].

The cyclization has also been effected by trifluoroacetic acid [197], hot acetic acid [197], and silica gel [198].

Jones reagent-induced oxidative spirocyclization of **386** to a γ-lactone **387** has been reported (Scheme 91) [199].

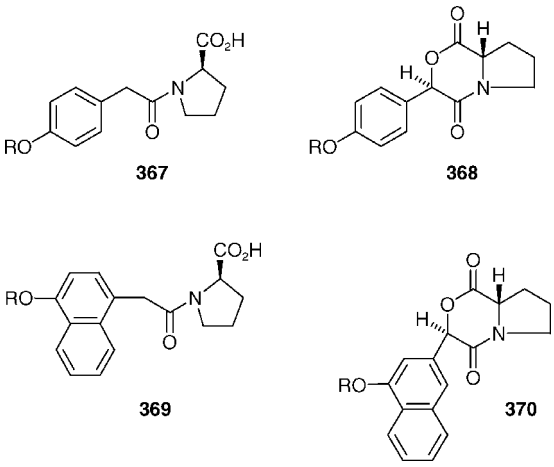


SCHEME 83



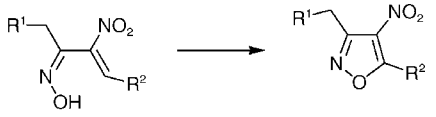
365 **366**

SCHEME 84



367 **368** **369** **370**

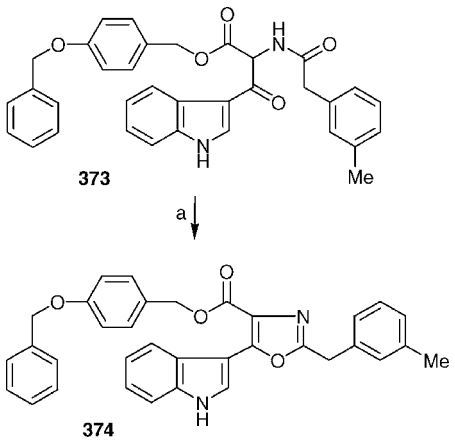
SCHEME 85



371 **372**

R1, R2= alkyl or aryl

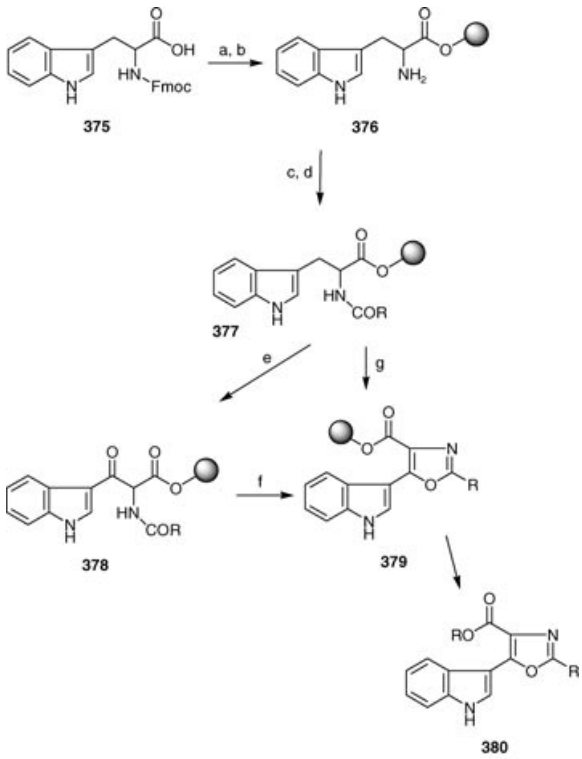
SCHEME 86



373 **374**

a. DDQ, Ph_3P, Et_3N, MeCN, CCl_4, r.t.

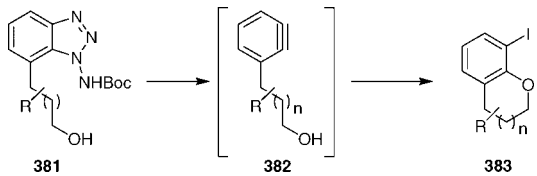
SCHEME 87



375 **376** **377** **378** **379** **380**

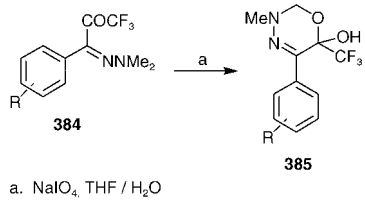
a. DIC, DMAP, DMF, r.t., 20h. b. piperidine / DMF, r.t., 2h. c. RCOOH, DIC, DMF, r.t., 20h. d. $(RCO)_2O$, py, r.t., 20h. e. DDQ, THF, H_2O, r.t., 20min. f. Ph_3P, Et_3N, CCl_4, MeCN, r.t., 2h. g. 20% TFA / CH_2Cl_2, r.t., 20min.

SCHEME 88



381 **382** **383**

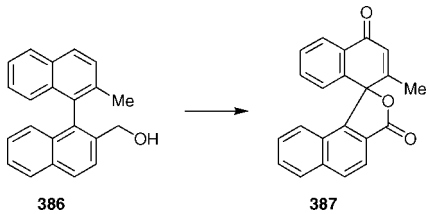
SCHEME 89



384 **385**

a. $NaIO_4$, THF / H_2O

SCHEME 90



386 **387**

SCHEME 91

It has been mentioned earlier (see, Schemes 70 and 72) that 1,5- and 1,6-dienes undergo oxidative cyclization to substituted THF and THP rings. This cyclization has also been effected with $KMnO_4$ [200] and recently by phase-transfer conditions, as an oxidation variant, with this reagent [201]. The syntheses of *cis*-solamin and its diastereoisomer have been recently described [202]. The key step in the reaction sequence is a $KMnO_4$ oxidative cyclization of a 1,5-diene to create the THF diol core, introducing all stereocenters in one step.

N-Bromosuccinimide (NBS) or 2,4,4,6-tetrabromo-cyclo-hexa-2,5-dien-1-one (TBB) have been successfully applied to oxidative ring closure of hydrazones **388** to 1,2,3-triazolo[1,5-*b*]isoquinolinium salts **389** (Scheme 92) [203].

Bromination leading to **390** can be avoided by using the stoichiometrically required oxidant for the ring closure.

Some quinoline alkaloids **399–403** have been obtained by *m*-chloroperbenzoic acid (*m*-CPBA) oxidative cyclization of **397** through an epoxide **398** and its subsequent ring-opening and cyclization to **399** and **400** and eventually to **401** and **403** (Scheme 93) [204].

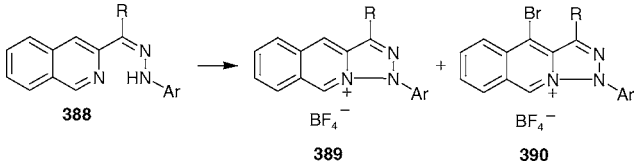
The Schiff base derivative **406**, prepared from the respective 5,6-diaminouracil **404** and aldehydes **405**, can be converted into the C-8 substituted xanthines **407** through an oxidative cyclization with *m*-CPBA (Scheme 94) [205].

Amides **408** have been oxidatively cyclized to the tetrahydroquinoline skeleton **410** by *t*-BuOCl/AgCl/CF_3CO_2H (Scheme 95) [206].

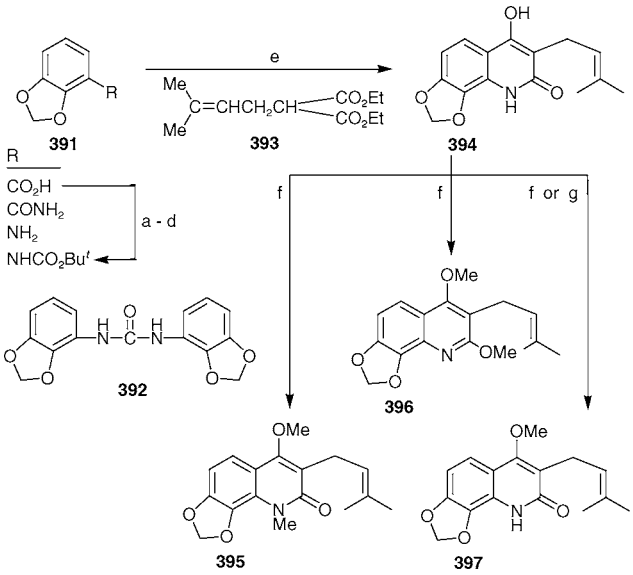
The oxidative cyclization has also been effectively accomplished by PIFA [206]. 1,2,4-Triazenes have been readily cyclized to 1,2,4-triazoles by a variety of oxidants such as NaOCl [207], $Ca(OCl)_2$ [208], TPAP/NMO [209] (see Schemes 63 and 76).

The core of methods used for the synthesis of 1,2,5-oxadiazole 2-oxides **413** is based on the cyclization of 1,2-dioximes **412** (Scheme 96) [210].

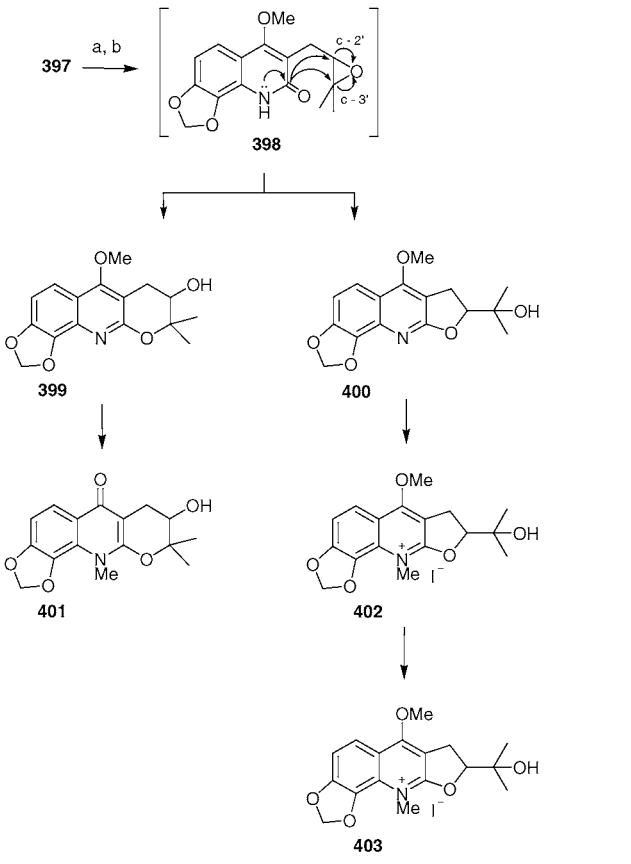
The unstable oxadiazole *N*-oxide **415**, produced by the action of dinitrogen tetroxide on the oxime



SCHEME 92

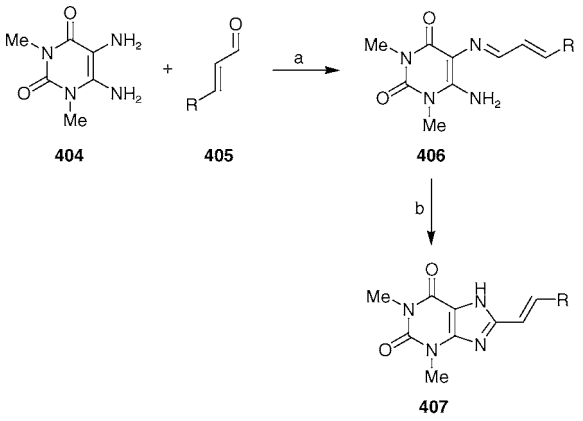


a. DPPA. b. Et_3N. c. Bu'OH. d. reflux in 1,4-dioxane. e. reflux in Ph_2O. f. 4 mol equiv. CH_2N_2, 6h. g. 10 mol equiv. CH_2N_2, 1min.



a. *m*-$ClC_6H_4CO_3H$. b. stir in dry $CHCL_3$, room temp., 40h. c. reflux in MeI, 15h. d. heat in pyridine, 85 - 90 °C, 3h

SCHEME 93



a. EtOH b. *m*-CPBA, MeCN

SCHEME 94

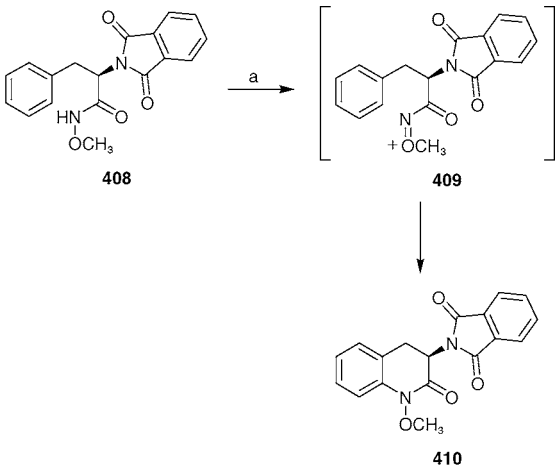
414, decomposes to the tricyclic oxadiazole derivative **416** in hot benzene [211]. The synthesis of the "pernitro compound," 3,4-dinitrofuroxan **417**, has been described (Scheme 97) [212].

The action of chloramine T on the acylhydrazones **418** (R^1, R^2 = aryl or 2-furyl) generates nitrile imines **419**, which undergo a 1,5-dipolar electrocyclization to the 1,3,4-oxadiazoles **420** (Scheme 97) [213].

NaOCl [214] and N_2O_4 [215] are among the most commonly used reagents for the oxidative cyclization of **412**.

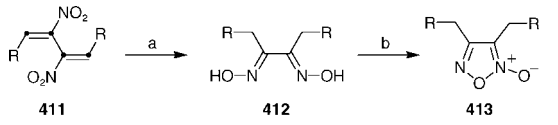
A similar approach is used for the synthesis of 1,2,3-triazole 1-oxides **423** from their oxime hydrazones **422** (Scheme 98) [214].

NaOCl or NaOBr are commonly used oxidants for the cyclization of 1,3-dioximes **424** to



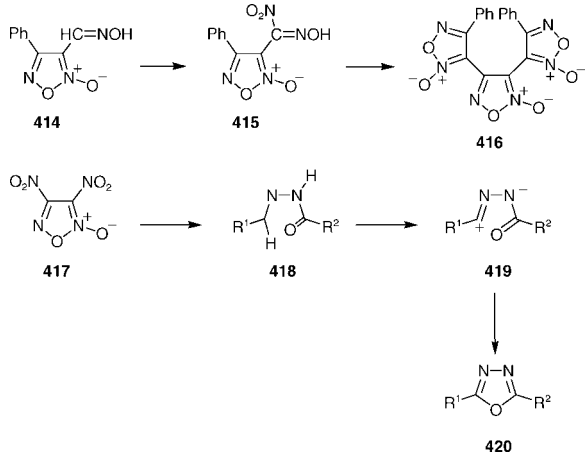
a. t-BuOCl; Ag(I)

SCHEME 95

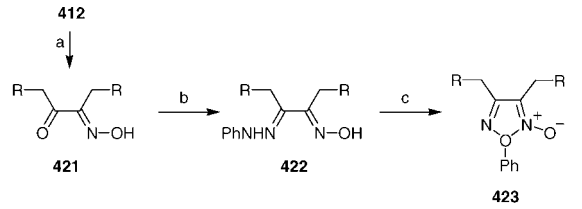


a. DMF-AcOH / Pb powder. b. EtOH / NaOH / 5% aq., NaClO

SCHEME 96

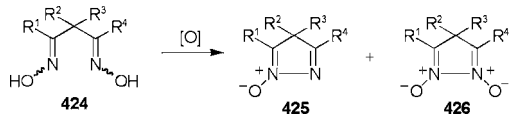


SCHEME 97

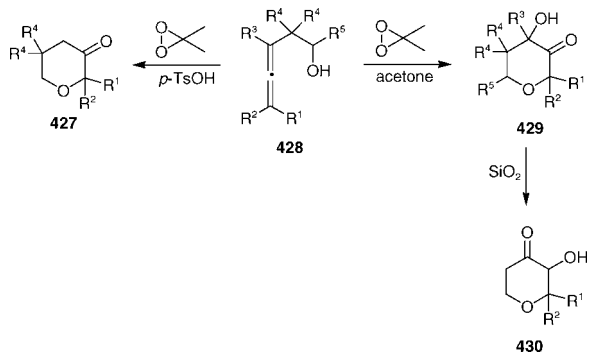


a. Dioxane, dil HCl, reflux. b. $PhNHNH_2$ in EtOH / AcOH, reflux.
c. Method A: N-iodosuccinimide in CCl_4, reflux; method B: $CuSO_4$ in aq. pyridine, reflux.

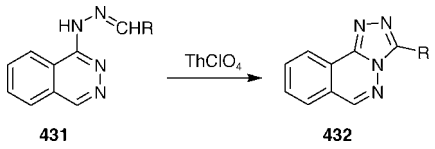
SCHEME 98



SCHEME 99



SCHEME 100



431 432

SCHEME 101

pyrazole 1-oxides **425** and pyrazole 1,2-dioxides **426** (Scheme 99) [216].

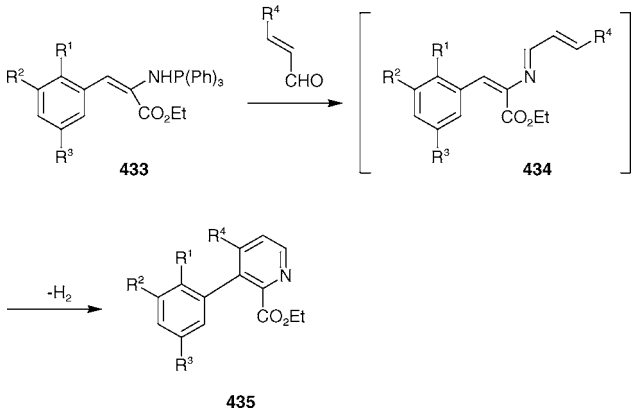
LTA and PIFA have also been effective for this cyclization.

The oxidation of β-allenyl alcohols **428** by dimethyldioxirane leads to functionalized tetrahydropyran-3-ones **429** in high yield, presumably via a spiro-dioxide derivative [217]. Under acidic conditions, a competitive cyclization leads to the simple pyran-3-one **427**. Examples of **429** substituted only at the 2-position undergo a ketol rearrangement on silica gel to the more stable pyran-4-one **430** (Scheme 100).

Hydrazones of phthalazines **431** undergo oxidative cyclization with thianthrene cation radical to furnish *s*-triazolo[3,4-*a*]phthalazines **432** (Scheme 101) [218].

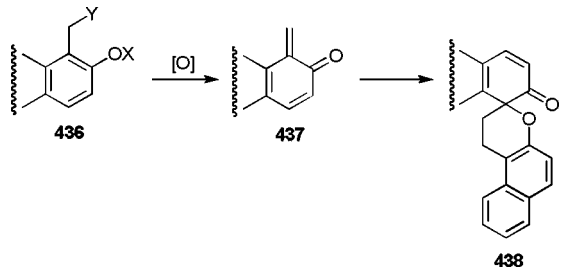
3-Arylpyridines **434** and **435** are made by electrocyclic ring closure of 3-azahexa-1,3,5-trienes **433** (Scheme 102) [219].

Oxidatively generated *o*-quinone methides **437** (Scheme 103) [220] and nitrile oxides **439** (Scheme 104) [221] by a variety of oxidants (many of which are already covered in this section) followed by spontaneous intermolecular cyclodimerization, in the absence of external interference, give rise to spiropyrans **438** and 1,2,5-oxadiazole 2-oxides **440**.



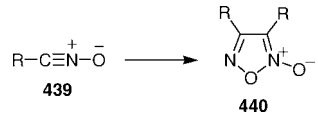
433 434 435

SCHEME 102



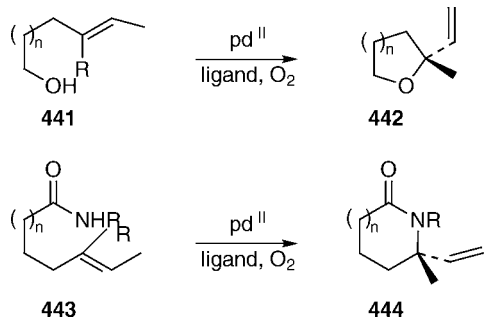
436 437 438

SCHEME 103



439 440

SCHEME 104



441 442 443 444

SCHEME 105

Pd-catalyzed aerobic oxidative heterocyclizations have been recently reported [222]. These constitute a conceptually and experimentally exciting approach to potentially valuable reactions exemplified by the transformations **441** to **442** and **443** to **444** (Scheme 105).

CONCLUSION

Oxidative cyclization will continue to serve actively organic synthesis more or less along the same lines. Perhaps some more oxidants will be included in the already rich arsenal in the near future. Apparently, the most promising expectations are on interesting transformations that may occur during the process.

REFERENCES

[1] Thebtaranonth, C.; Thebtaranonth, Y. Cyclization Reactions; CRC Press: London, 1994.

[2] (a) Gilchrist, T. L. Heterocyclic Chemistry, 3rd ed.; Longman: New York, 1997; (b) Gilchrist, T. L. J Chem Soc, Perkin Trans 1 2001, 2491 and references cited therein.

[3] (a) Katritzky, A. R.; Rees, C. W. Comprehensive Heterocyclic Synthesis; Academic Press: Oxford, 1984; (b) Katritzky, A. R.; Rees, C. W. Comprehensive Heterocyclic Chemistry-II; Academic Press: Oxford, 1996; (c) Katritzky, A. R.; Pozharskii, A. F. Handbook of Heterocyclic Chemistry, 2nd ed.; Pergamon: Oxford, 2000.

[4] Weissberger, A.; Taylor, E. C. Chemistry of Heterocyclic Compounds, A Series of Monographs; Wiley-Interscience.

[5] Albini, A.; Pietra, S. Heterocyclic N-Oxides; CRC Press: Boca Raton, FL, 1991.

[6] (a) Coldham, I. J Chem Soc, Perkin Trans 1 1998, 1343 and references cited therein; (b) Afarinkia, K. J Chem Soc, Perkin Trans 1 1999, 2025 and references cited therein.

[7] (a) Steel, P. G. J Chem Soc, Perkin Trans 1 2001, 2727 and references cited therein; (b) Hwu, J. R.; King, K. Y. Curr Sci 2001, 81, 1043 and references cited therein.

[8] (a) Tonks, L.; Williams, J. M. J. J Chem Soc, Perkin Trans 1 1998, 3637 and references cited therein; (b) Haughton, L.; Williams, J. M. J. J Chem Soc, Perkin Trans 1 1999, 2645 and references cited therein; (c) Haughton, L.; Williams, J. M. J. J Chem Soc, Perkin Trans 1 2000, 3335 and references cited therein.

[9] (a) Donohoe, T.; Harji, J. R. R.; Moore, P. R.; Waring, M. J. J Chem Soc, Perkin Trans 1 1998, 819 and references cited therein; (b) Comely, A. C.; Gibson, S. E. J Chem Soc, Perkin Trans 1 1999, 223 and references cited therein; (c) Comely, A. C.; Gibson, S. E.; Sur, S. J Chem Soc, Perkin Trans 1 2000, 109 and references cited therein; (d) Fletcher, A. J.; Christie, S. D. R. J Chem Soc, Perkin Trans 1 2001, 1 and references cited therein.

[10] Fletcher, A. J.; Christie, S. D. R. J Chem Soc, Perkin Trans 1 2000, 1657 and references cited therein.

[11] Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. Chem Rev 1996, 96, 635 and references cited therein.

[12] (a) Poli, G.; Giambastiani, G.; Heumann, A. Tetrahedron 2000, 56, 5959 and references cited therein; (b) Prim, D.; Campagne, J.-M.; Joseph, D.; Andrioletti, B. Tetrahedron 2002, 58, 2041 and references cited therein.

[13] Naota, T.; Takaya, H.; Murahashi, S.-I. Chem Rev 1998, 98, 2599 and references cited therein.

[14] Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. Acc Chem Res 1998, 31, 805 and references cited therein.

[15] (a) Larock, R. C. J Organomet Chem 1999, 576, 111 and references cited therein; (b) Bateson, J. H.; Mitchell, M. B. Organometallic Reagents in Organic Synthesis; Academic Press: London, 1994; (c) McQuillin, F. J.; Parker, D. G.; Stephenson, G. R. Transition Metal Organometallics for Organic Synthesis; Cambridge University Press: Cambridge, England, UK, 1991.

[16] Yang, B. H.; Buchwald, S. L. J Organomet Chem 1999, 576, 125 and references cited therein.

[17] (a) Trost, B. M.; Shi, Y. J Am Chem Soc 1993, 115, 9421; (b) Negishi, E.; Copéret, C.; Ma, S.; Lion, S. Y.; Liu, F. Chem Rev 1996, 96, 365.

[18] Montgomery, J.; Sco, J. Tetrahedron 1998, 54, 1131.

[19] (a) Annual Reports on the Progress of Chemistry, Section B, Organic Chemistry; Royal Society of Chemistry: UK, 1990; Vol. 87 until 2002; Vol. 98; (b) Progress in Heterocyclic Chemistry; Pergamon: Oxford, 1990; Vol. 3 until 2002; Vol. 14.

[20] See Ref. [19] for relevant literature.

[21] (a) Collins, I. J Chem Soc, Perkin Trans 1 2000, 2845; (b) Collins, I. J Chem Soc, Perkin Trans 1 2002, 1921.

[22] Geysen, M. Chem Biol 1998, 5, 265 and references cited therein.

[23] (a) Balkenhohl, F.; von dem Bussche-Hünnefeld, C.; Lansky, A.; Zechel, C. Angew Chem, Int Ed Engl 1996, 35, 2288 and references cited therein; (b) Thompson, L. A.; Ellman, J. A. Chem Rev 1996, 96, 555 and references cited therein; (c) Nefzi, A.; Ostresh, J. M.; Haughten, R. A. Chem Rev 1997, 97, 449 and references cited therein; (d) Loughlin, W. A. Aust J Chem 1998, 51, 875 and references cited therein; (e) Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, R. I.; Taylor, S. J. J Chem Soc, Perkin Trans 1 2000, 3815 and references cited therein; (f) Krchňak, V.; Holladay, M. W. Chem Rev 2002, 102, 61 and references cited therein.

[24] (a) Lehn, J.-M. Chem Eur J 1999, 5, 2455 and references cited therein; (b) Kirschning, A.; Monenshein, H.; Wittenberg, R. Chem Eur J 2000, 6, 4445 and references cited therein; (c) Yoshida, J.-i.; Suga, S. Chem Eur J 2002, 8, 2651 and references cited therein; (d) Bienaymé, H.; Hulme, C.; Oddon, G.; Schmitt, P. Chem Eur J 2000, 6, 3321 and references cited therein.

[25] Smith, M. B.; March, J. Advanced Organic Chemistry: Reactions, Mechanisms and Structure, 5th ed.; Wiley Interscience: New York, 2001; p. 1506.

[26] Kusama, H.; Uchiyama, K.; Yamashita, Y.; Narasaka, K. Chem Lett 1995, 715.

[27] Kusama, H.; Yamashita, Y.; Narasaka, K. Chem Lett 1995, 5.

[28] (a) Mori, K.; Takahashi, M.; Yamamura, S.; Nishiyama, S. Tetrahedron 2001, 57, 5527; (b) Mori, K.; Yamamura, S.; Nishiyama, S. Tetrahedron 2001, 57, 5533.

[29] Yoshida, J.-i.; Ishichi, Y.; Isoe, S. J Am Chem Soc 1992, 114, 7594.

[30] Yoshida, J.-i.; Takada, K.; Ishichi, Y.; Isoe, S. J Chem Soc, Chem Commun 1994, 2361.

[31] Tin and silicon have recently been used as effective "electro-auxiliaries" in electroorganic synthesis. For examples see (a) Yoshida, J.-i.; Isoe, S. Tetrahedron Lett 1987, 28, 6621; (b) Yoshida, J.-i.; Itoh, M.; Isoe, S. J Chem Soc, Chem Commun 1993, 547; (c) Suda, K.; Hotoda, K.; Watanabe, J.; Shiozawa, K.; Takahami, T. J Chem Soc, Perkin Trans 1 1992, 1283.

[32] (a) Yoshida, J.-i.; Matsunaga, S.; Murata, T.; Isoe, S. Tetrahedron 1991, 47, 615; (b) Koizumi, T.; Fuchigami, T.; Nonaka, T. Chem Express 1986, 1, 355.

[33] (a) Varvoglis, A.; Spyroudis, S. Synlett 1998, 221 and references cited therein; (b) Vargolis, A. Hypervalent Iodine in Organic Synthesis; Academic Press: San Diego, 1996; (c) Wirth, T.; Hirt, U. Synthesis 1999, 1271; (d) Moriarty, R. M.; Prakash, O. Adv Heterocycl Chem 1998, 69, 1 and references cited therein.
[34] Finet, J.-P. Tetrahedron Organic Chemistry Series: Ligand Coupling Reactions with Heteroatomic Compounds, Pergamon: Oxford, 1998; Vol. 18.
[35] Brimble, M. A.; Williams, G. M. J Org Chem 1992, 57, 5818.
[36] Kacan, M.; Koyuncu, D.; McKillop, A. J Chem Soc, Perkin Trans 1 1993, 1771.
[37] (a) Noda, H.; Niwa, M.; Yamamura, S. Tetrahedron Lett 1981, 22, 3247; (b) Nishiyama, S.; Yamamura, S. Tetrahedron Lett 1983, 24, 3351.
[38] (a) McKillop, A.; McLaren, L.; Taylor, R. J. K.; Watson, R. J.; Lewis, N. Synlett 1992, 201; (b) Plourde, G. L. Tetrahedron Lett 2002, 43, 3597.
[39] (a) Murakata, M.; Yamada, K.; Hoshino, O. J Chem Soc, Chem Commun 1994, 443; (b) Murakata, M.; Yamada, K.; Hoshino, O. Tetrahedron 1996, 52, 14713; (c) Murakata, M.; Tamura, M.; Hoshino, O. J Org Chem 1997, 62, 4428; (d) Murakata, M.; Yamada, K.; Hoshino, O. Heterocycles 1998, 47, 921.
[40] Kotali, A.; Harris, P. A. J Heterocycl Chem 1996, 33, 605.
[41] Yang, R.-Y.; Dai, L.-X. J Org Chem 1993, 58, 3381.
[42] Varma, R. S.; Saini, R. K.; Prakash, O. Tetrahedron Lett 1997, 38, 2621.
[43] Srivastava, R. G.; Venkataramani, P. S. Synth Commun 1988, 18, 1537.
[44] Stevens, F. F.; Bower, J. D. J Chem Soc 1949, 2971.
[45] Nakagawa, K.; Onoue, H.; Sugita, J. J Chem Pharm Bull 1964, 12, 1135.
[46] Speier, G. J Mol Catal 1987, 41, 253.
[47] Park, K. H.; Jun, K.; Shin, S. R.; Oh, S. W. Tetrahedron Lett 1996, 37, 8869.
[48] Prakash, O.; Gujral, H. K.; Rani, N.; Singh, S. P. Synth Commun 2000, 30, 417.
[49] Patel, H. V.; Vyas, K. A.; Pandey, S. P.; Tavares, F.; Fernandes, P. S. Synth Commun 1991, 21, 1583.
[50] Pelter, A.; Hussain, A.; Smith, G.; Ward, R. S. Tetrahedron 1997, 53, 3879.
[51] Yu, C.; Jiang, Y.; Lin, B.; Hu, L. Tetrahedron Lett 2001, 42, 1449.
[52] Bolshakov, A. V.; Ganina, O. G.; Shavirin, A. S.; Kurskii, Y. A.; Finet, J.-P.; Yu Fedorov, A. Tetrahedron Lett 2002, 43, 8245.
[53] Espino, C. G.; Du Bois, J. Angew Chem, Int Ed Engl 2001, 40, 598.
[54] Takacs, J. M.; Jaber, M. R.; Vellekoop, A. S. J Org Chem 1998, 63, 2742.
[55] Ishizuka, T.; Kunieda, T. Tetrahedron Lett 1987, 28, 4185.
[56] Prakash, O.; Gujral, H. K.; Rani, N.; Singh, S. P. Synth Commun 2000, 30, 417.
[57] Yang, R.; Dai, L. J Org Chem 1993, 58, 3381.
[58] (a) Ahn, Y.; Cardenas, G. I.; Yang, J.; Romo, D. Org Lett 2001, 3, 751; (b) Mecozzi, T.; Petrini, M. Synlett 2000, 74 and references cited therein.
[59] (a) Dess, D. B.; Martin, J. C. J Am Chem Soc 1991, 113, 7277; (b) Meyer, S. D.; Schreiber, S. L. J Org Chem 1994, 59, 7549.
[60] Yu, C.; Hu, L. Tetrahedron Lett 2001, 42, 5167.
[61] (a) Takada, T.; Arisawa, M.; Gyoten, M.; Hamada, R.; Tohma, H.; Kita, Y. J Org Chem 1998, 63, 7698; (b) Kita, Y.; Gyoten, M.; Otsubo, M.; Takada, H. Chem Commun 1996, 1481.
[62] Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Sugita, K. J Am Chem Soc 2002, 124, 2212.
[63] (a) Frigerio, M.; Santagostino, M.; Sputore, S. J Org Chem 1999, 64, 4537; (b) Katritzky, A. R.; Duell, B. L.; Gallos, J. K. Org Magn Reson 1989, 27, 1007; (c) Frigerio, M.; Santagostino, M. Tetrahedron Lett 1994, 35, 8019; (d) Corey, E. J.; Palani, A. Tetrahedron Lett 1995, 36, 7945.
[64] Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Barluenga, S.; Hunt, K. W.; Kranich, R.; Vega, J. A. J Am Chem Soc 2002, 124, 2233.
[65] Green, I. R.; Hugo, V. I.; Oosthuisen, F. J.; van Eeden, N.; Giles, R. G. F. S Afr J Chem 1995, 48, 15.
[66] De Koning, C. B.; Green, I. R.; Michael, J. P.; Oliveira, J. R. Tetrahedron Lett 1997, 38, 5055.
[67] McKillop, A.; Taylor, E. C. In Comprehensive Organometallic Chemistry; Wilkinson, J. (Ed.); Pergamon: Oxford, 1982; Vol. 7, pp. 465–513.
[68] Mohamed, S. E. N.; Thomas, P.; Whiting, D. A. J Chem Soc, Perkin Trans 1 1987, 431.
[69] Levai, A.; Tokes, A. L. Synth Comm 1982, 12, 701.
[70] Horie, T.; Yamada, T.; Kawamura, Y.; Tsukayama, M.; Kuramoto, M. J Org Chem 1992, 57, 1038.
[71] (a) Thakkar, K.; Cushman, M. Tetrahedron Lett 1994, 35, 6441; (b) Thakkar, K.; Cushman, M. J Org Chem 1995, 60, 6499.
[72] Kamara, B. I.; Brandt, E. V.; Ferreira, D. Tetrahedron 1999, 55, 861.
[73] Singh, O. V.; Muthukrishnan, M.; Sundaravadivelu, M. Indian J Chem, Sect B 2001, 40B, 263.
[74] (a) Mihailović, M. L.; Ćeković, Z.; Lorenc, L. Organic Syntheses by Oxidation with Metal Compounds; Mijs, W. J.; de Jonge, C. R. H. I. (Eds.); Plenum: New York, 1986; (b) Criegee, R. Angew Chem 1985, 70, 173; (c) Mihailović, M. L.; Ćeković, Z. Synthesis 1970, 209.
[75] Tsunoi, S.; Ryu, I.; Sonoda, N. J Am Chem Soc 1994, 116, 5473.
[76] Curran, D. P.; Shen, W. J Am Chem Soc 1993, 115, 6051.
[77] Bathini, Y.; Lown, J. W. Synth Commun 1991, 21, 215.
[78] Yamamoto, Y.; Ohno, H.; Eguchi, S. J Am Chem Soc 1995, 117, 9653.
[79] Hadjantoniou-Maroulis, C. P.; Ikonomou, V.; Parisopoulou, E. J Heterocycl Chem 1996, 33, 655.
[80] Kaihoh, T.; Itoh, T.; Yamaguchi, K.; Ohsawa, A. J Chem Soc, Chem Commun 1988, 1608.
[81] Kaihoh, T.; Itoh, T.; Yamaguchi, K.; Ohsawa, A. J Chem Soc, Perkin Trans 1 1991, 2045.
[82] Boulton, A. J.; Fruttero, R.; Saka, D. K.; Williams, M. T. J Chem Soc, Perkin Trans 1 1986, 1249.
[83] Maroulis, A. J.; Domzaridou, K. C.; Hadjantoniou-Maroulis, C. P. Synthesis 1998, 1769.
[84] Kotali, A.; Lazaridou, E.; Papageorgiou, V.; Harris, P. A. Heterocycles 2001, 55, 1057.
[85] (a) Supsana, P.; Tsoungas, P. G.; Varvounis, G. Tetrahedron Lett 2000, 41, 1845; (b) Supsana, P.; Tsoungas, P. G.; Aubry, A.; Skoulika, S.; Varvounis, G. Tetrahedron 2001, 57, 3445.
[86] (a) Tsoungas, P. G. Heterocycles 2002, 57, 915 and

references cited therein; (b) Tsoungas, P. G. Heterocycles 57, 1149 and references cited therein.
[87] Musič, I.; Verček, B. Synth Commun 2001, 31, 1511.
[88] Hegedus, L. S. Organometallics in Synthesis; Schlosser, M. (Ed.); Wiley: Chichester, UK, 1994.
[89] Li, J. J.; Gribble, G. W. Tetrahedron Organic Chemistry Series: Palladium in Heterocyclic Chemistry; Pergamon: Oxford, 2000; Vol. 20.
[90] Hall, R. J.; Marchant, J.; Oliveira-Campos, A. M. F.; Queiroz, M.-J. R. P.; Shannon, P. V. R. J Chem Soc, Perkin Trans 1 1992, 3439.
[91] (a) Knölker, H.-J.; O'Sullivan, N. Tetrahedron 1994, 50, 1695; (b) Knölker, H.-J.; O'Sullivan, N. Tetrahedron 1994, 50, 10893.
[92] Mithani, S.; Weeratunga, G.; Taylor, N. J.; Dmitrienko, G. I. J Am Chem Soc 1994, 116, 2209.
[93] Hagelin, H.; Oslob, J. D.; Åkermark, B. Chem Eur J 1999, 5, 2413.
[94] Åkermark, B.; Oslob, J. D.; Heuschert, U. Tetrahedron Lett 1995, 1325.
[95] Bäckwall, J.-E. Palladium-Catalysed 1,4-Additions to Conjugated Dienes in Metal-Catalysed Cross-Coupling Reactions; Stang, P.; Diederich, F. (Eds.); Wiley-VCH: Weinheim, 1998.
[96] Itami, K.; Palmgren, A.; Bäckwall, J.-E. Tetrahedron Lett 1998, 39, 1223.
[97] Hosokawa, T.; Murahashi, S.-I. Heterocycles 1992, 33, 1079 and references cited therein.
[98] (a) Bäckwall, J.-E.; Andersson, P. G. J Am Chem Soc 1990, 112, 3683; (b) Bäckwall, J.-E.; Andersson, P. G. J Org Chem 1991, 56, 2274; (c) Bäckwall, J.-E.; Andersson, P. G.; Stone, G. B.; Gogoll, A. J Org Chem 1991, 56, 2988; (d) Andersson, P. G.; Bäckwall, J.-E. J Org Chem 1991, 56, 5349; (e) Andersson, P. G.; Bäckwall, J.-E. J Am Chem Soc 1992, 114, 8696; (f) Bäckwall, J.-E.; Granberg, K. L.; Andersson, P. G.; Gatti, R.; Gogoll, A. J Org Chem 1993, 58, 5445; (g) Andersson, P. G.; Nilsson, Y. I. M.; Bäckwall, J.-E. Tetrahedron 1994, 50, 559; (h) Koroleva, E. B.; Bäckwall, J.-E.; Andersson, P. G. Tetrahedron Lett 1995, 36, 5397; (i) Nilsson, Y. I. M.; Aranyos, A.; Andersson, P. G.; Bäckwall, J.-E.; Parrain, J. L.; Ploteau, C.; Quintard, J. P. J Org Chem 1996, 61, 1825; (j) Bäckwall, J.-E.; Andersson, P. G. J Am Chem Soc 1992, 114, 6374.
[99] (a) Friestad, G. K.; Branchaud, B.-P. Tetrahedron Lett 1995, 36, 7047; (b) Ponaras, A. A.; Zaim, Ö. Tetrahedron Lett 1993, 34, 2879.
[100] (a) Hosokawa, T.; Uno, T.; Inui, S.; Murahashi, S.-I. J Am Chem Soc 1981, 103, 2318; (b) Hosokawa, T.; Okuda, C.; Murahashi, S.-I. J Org Chem 1985, 50, 1282.
[101] Uozumi, Y.; Kato, K.; Hayashi, T. J Am Chem Soc 1997, 119, 5063.
[102] Miura, M.; Tsuda, T.; Satoh, T.; Nomura, M. Chem Lett 1997, 1103.
[103] (a) Fujiwara, Y.; Jintoku, T.; Takaki, K. CHEMTECH 1990, 636; (b) Tsuji, J. Palladium Reagent and Catalysts; Wiley: Chichester, UK, 1995; pp. 55–59.
[104] (a) Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N.; Murai, S. Bull Chem Soc Jpn 1995, 68, 62; (b) Chatani, N.; Kakiuchi, Y. Ie. F.; Murai, S. J Org Chem 1997, 62, 2604; (c) Lim, Y.-G.; Kang, J.-B.; Kim, Y. H. J Chem Soc, Perkin Trans 1 1996, 2201 and references cited therein.
[105] Larock, R. C.; Hightower, T. R.; Hasvold, L. A.; Peterson, K. P. J Org Chem 1996, 61, 3584.
[106] Deshpande, P. P.; Martin, O. R. Tetrahedron Lett 1990, 31, 6313.
[107] Bringmann, G.; Breuning, M.; Tasler, S. Synthesis 1999, 525 and references cited therein.
[108] (a) Bringmann, G.; Francois, G.; Aké, L. A.; Schlauer, J. Chimia 1998, 52, 18; (b) Bringmann, G.; Rübenacker, M.; Jansen, J. R.; Scheutzow, D.; Aké, L. A. Tetrahedron Lett 1990, 31, 639; (c) Bringmann, G.; Jansen, J. R.; Reuscher, H.; Rübenacker, M.; Peters, K.; von Schnering, H. G. Tetrahedron Lett 1990, 31, 643.
[109] Giles, R. G. F.; Green, I. R.; Taylor, C. P. Tetrahedron Lett 1999, 40, 4871.
[110] (a) Hennings, D. D.; Iwasa, S.; Rawal, V. H. J Org Chem 1997, 62, 2; (b) Miura, M.; Tsuda, T.; Satoh, T.; Nomura, M. Chem Lett 1997, 1103; (c) Emoto, T.; Kubosaki, N.; Yamagiwa, Y.; Kamikawa, T. Tetrahedron lett 2000, 41, 355.
[111] (a) Song, J. J.; Yee, N. K. Org Lett 2000, 2, 519; (b) Song, J. J.; Yee, N. K. Tetrahedron Lett 2001, 42, 2937.
[112] Fan, P.; Ablordeppey, S. Y. J Heterocycl Chem 1997, 34, 1789.
[113] (a) Snider, B. B. Chem Rev 1996, 96, 339 and references cited therein; (b) Melikyan, G. G. Org React 1997, 49, 427; (c) Melikyan, G. G. Aldrichimica Acta 1998, 31, 50; (d) Snider, B. B. Radicals in Organic Synthesis; Renaud, P.; Sibi, M. (Eds.); Wiley-VCH: Weinheim, 2001; Vol. 1, Ch. 2.3, pp. 198–213.
[114] Chuang, C.-P.; Wu, Y.-L.; Jiang, M.-C. Tetrahedron 1999, 55, 11229.
[115] (a) Mahamat, H. O.; Moustrou, C.; Surzur, J.-M.; Bertrand, M. P. J Org Chem 1989, 54, 5684; (b) Snider, B. B.; Che, Q. Tetrahedron 2002, 58, 7821.
[116] Knölker, H.-J.; Bauermeister, M.; Pannek, J.-B.; Bläser, D.; Boese, R. Tetrahedron 1993, 49, 841.
[117] (a) Knölker, H.-J.; Bauermeister, M. Helv Chim Acta 1993, 76, 2500; (b) Knölker, H.-J.; Bauermeister, M.; Pannek, J.-B.; Wolpert, M. Synthesis 1995, 397; (c) Knölker, H.-J.; Baum, E.; Hopfmann, T. Tetrahedron Lett 1995, 36, 5339; (d) Knölker, H.-J.; Hopfmann, T. Synlett 1995, 981; (e) Knölker, H.-J.; Fröhner, W. Tetrahedron Lett 1998, 2537.
[118] Knölker, H.-J.; Budei, F.; Pannek, J.-B.; Schlechtingen, G. Synlett 1996, 587.
[119] Davies, D.; Kapur, N.; Parsons, A. F. Tetrahedron Lett 1998, 39, 4397.
[120] Kirillova, L. P.; Shuigina, V. M.; Shafeev, M. A.; Al'mukhamedov, A. A.; Vereshchagin, L. I. Zh Org Khim 1996, 32, 1089.
[121] Crombie, B. S.; Redhouse, A. D.; Smith, C.; Wallace, T. W. J Chem Soc, Chem Commun 1995, 403.
[122] (a) Bar, G.; Parsons, A. F.; Thomas, C. B. Tetrahedron Lett 2000, 41, 7751; (b) Bar, G.; Parsons, A. F.; Thomas, C. B. Tetrahedron 2001, 57, 4719.
[123] Cherkaoui, M. Z.; Scherowsky, G. New J Chem 1997, 21, 1203.
[124] Vyskočil, S.; Snirčina, M.; Lorenc, M.; Tišlerova, I.; Brooks, R. D.; Kulagowski, J. J.; Langer, V.; Farrugia, L. J.; Kočovsky, P. J Org Chem 2001, 66, 1359.
[125] Sabnis, R. W.; Rangnekar, D. W. J Heterocycl Chem 1991, 28, 1105.

[126] Sabnis, R. W.; Rangnekar, D. W. J Heterocycl Chem 1990, 27, 417.
[127] Alcazar, J.; Almena, I.; Begtrup, M.; De la Hoz, A. J Chem Soc, Perkin Trans 1 1995, 2773.
[128] Uhlmann, P.; Felding, J.; Vedsø, P.; Begtrup, M. J Org Chem 1997, 62, 9177.
[129] Martinez, E.; Martinez, L.; Estévez, J. C.; Estévez, R. J.; Castedo, L. Tetrahedron Lett 1998, 39, 2175.
[130] Berge, J.; Claridge, S.; Mann, A.; Muller, C.; Tyrrell, E. Tetrahedron Lett 1997, 38, 685.
[131] Bhandal, H.; Patel, V. F.; Pattenden, G.; Russell, J. J. J Chem Soc, Perkin Trans 1 1990, 2691.
[132] Hari, A.; Karan, C.; Rodrigues, W. C.; Miller, B. L. J Org Chem 2001, 66, 991.
[133] Knölker, H.-J.; Baum, G.; Pannek, J.-B. Tetrahedron 1996, 52, 7345.
[134] Ali, A. S.; Wilkie, J. S.; Winzenberg, K. N. Aust J Chem 1997, 50, 911.
[135] Aubert, C.; Buisine, O.; Malacria, M. Chem Rev 2002, 102, 813 and references cited therein.
[136] Mruthyunjayaswamy, B. H. M.; Shanthaveerappa, B. K. Indian J Heterocycl Chem 1998, 8, 31.
[137] Naota, T.; Murahashi, S.-I. Synlett 1991, 693.
[138] (a) Murahashi, S.-I.; Ito, K.; Naota, T.; Maeda, Y. Tetrahedron Lett 1981, 22, 5327; (b) Murahashi, S.-I.; Naota, T.; Ito, K.; Maeda, Y.; Taki, H. J Org Chem 1987, 52, 4319; (c) Ishii, Y.; Osakada, K.; Ikariya, T.; Saburi, M.; Yoshikawa, S. J Org Chem 1986, 51, 2034.
[139] Blum, Y.; Shvo, Y. J Organomet Chem 1985, 282, C7.
[140] Shvo, Y.; Blum, Y.; Reshef, D.; Menzin, M. J Organomet Chem 1982, 226, C21.
[141] Ishii, Y.; Ikariya, T.; Saburi, M.; Yoshikawa, S. Tetrahedron Lett 1986, 27, 365.
[142] Saburi, M.; Ishii, Y.; Kaji, N.; Aoi, T.; Sasaki, I.; Yoshikawa, S.; Uchida, Y. Chem Lett 1989, 563.
[143] (a) Nozaki, K.; Yoshida, M.; Takaya, H. J Organomet Chem 1994, 473, 253; (b) Ji, H.; Mizugaki, T.; Ebitani, K.; Kaneda, K. Tetrahedron Lett 2002, 43, 7179.
[144] Naota, T.; Takaya, H.; Murahashi, S.-I. Chem Rev 1998, 98, 2599 and references cited therein.
[145] Robin, J.-P.; Landais, Y. J Org Chem 1988, 53, 224.
[146] (a) Landais, Y.; Robin, J.-P. Tetrahedron Lett 1986, 27, 1785; (b) Landais, Y.; Lebrun, A.; Robin, J.-P. Tetrahedron Lett 1986, 27, 5377; (c) Landais, Y.; Rambault, D.; Robin, J.-P. Tetrahedron Lett 1987, 28, 543.
[147] Cho, C. S.; Kim, B. T.; Kim, T.-J.; Shim, S. C. Chem Commun 2001, 2576.
[148] Albarella, L.; Musumeci, D.; Sica, D. Eur J Org Chem 2001, 997.
[149] (a) Piccialli, V.; Sica, D.; Smaldone, D. Tetrahedron 1993, 49, 4211; (b) Notaro, G.; Piccialli, V.; Sica, D.; Smaldone, D. Tetrahedron 1994, 50, 4835; (c) Albarella, L.; Piccialli, V.; Sica, D.; Smaldone, D. J Chem Res, Synop 1996, 400.
[150] Piccialli, V. Tetrahedron Lett 2000, 41, 3731.
[151] (a) Tsuji, Y.; Kotachi, S.; Huh, K.-T.; Watanabe, Y. J Org Chem 1990, 55, 580; (b) Webb, R. R.; Venuti, M. C.; Eigenbrot, C. J Org Chem 1991, 56, 4706.
[152] (a) Sinha, S. C.; Sinha-Bagchi, A.; Keinan, E. J Am Chem Soc 1995, 117, 1447; (b) Sinha, S. C.; Keinan, E.; Sinha, S. C. J Am Chem Soc 1998, 120, 9076; (c) D'Souza, L. J.; Sinha, S. C.; Lu, S.-F.; Keinan, E.; Sinha, S. C. Tetrahedron 2001, 57, 5255.
[153] (a) Kusama, H.; Uchiyama, K.; Yamashita, Y.; Narasaka, K. Chem Lett 1995, 715; (b) Kusama, H.; Yamashita, Y.; Uchiyama, K.; Narasaka, K. Bull Chem Soc Jpn 1997, 70, 965; (c) Mori, S.; Uchiyama, K.; Hayashi, Y.; Narasaka, K.; Nakamura, E. Chem Lett 1998, 111.
[154] Donohoe, T. J.; Moore, P. R.; Waring, M. J.; Newcombe, N. J. Tetrahedron Lett 1997, 38, 5027.
[155] (a) Donohoe, T. J.; Blade, K.; Moore, P. R.; Winter, J. J. G.; Helliwell, M.; Stemp, G. J Org Chem 1999, 64, 2980; (b) Donohoe, T. J.; Blades, K.; Winter, J. J. G.; Stemp, G. Tetrahedron Lett 2000, 41, 4701.
[156] Donohoe, T. J.; Winter, J. W.; Helliwell, M.; Stemp, G. Tetrahedron Lett 2001, 42, 971.
[157] De Champdore, M.; Lasalvia, M.; Piccialli, V. Tetrahedron Lett 1998, 39, 9781.
[158] Brown, R. C. D.; Hughes, R. M.; Keily, J.; Kenney, A. J Chem Commun 2000,1735.
[159] Travis, B.; Borhan, B. Tetrahedron Lett 2001, 42, 7741.
[160] Kesteleyn, B.; De Kimpe, N.; Van Puyvelde, L. J Org Chem 1999, 64, 1173.
[161] (a) Paulvannan, K.; Chen, T.; Hale, R. Tetrahedron 2000, 56, 8071; (b) Buzykim, B.; Bredikhina, Z. A. Synthesis 1993, 59.
[162] Molander, G. A. Chem Rev 1992, 92, 28 and references cited therein.
[163] Snider, B. B.; Kwon, T. J Org Chem 1990, 55, 4786.
[164] Arai, N.; Narasaka, K. Bull Chem Soc Jpn 1997, 70, 2525.
[165] Durand, A.-C.; Dumez, E.; Rodriguez, J.; Dulcere, J.-P. Chem Commun 1999, 2437.
[166] (a) Boivin, T. L. B. Tetrahedron 1987, 43, 3309; (b) Perron, F.; Albizati, K. F. Chem Rev 1989, 89, 1617; (c) Cardillo, G.; Orena, M. Tetrahedron 1990, 46, 3321; (d) Kotsuki, H. Synlett 1992, 97; (e) Postena, M. H. D. Tetrahedron 1992, 48, 8545.
[167] (a) Rao, A. V. R.; Yadav, J. S.; Rao, C. S.; Chandrasekhar, S. J Chem Soc, Perkin Trans 1 1990, 1211; (b) Tang, J.; Shinokubo, H.; Oshima, K. Tetrahedron 1999, 55, 1893; (c) Dalla, V.; Pale, P. Tetrahedron Lett 1992, 33, 7857; (d) Audin, C.; Lancelin, J.-M.; Beau, J.-M. Tetrahedron Lett 1988, 29, 3691; (e) Suginome, M.; Iwanami, T.; Ito, Y. J Org Chem 1998, 63, 6096; (f) Shing, T. K. M.; Zhong, Y.-L.; Mak, T. C. W.; Wang, R.; Xue, F. J Org Chem 1998, 63, 414; (g) Cloninger, M. J.; Overman, L. E. J Am Chem Soc 1999, 121, 1092; (h) Craig, D.; King, N. P.; Shaw, A. N. Tetrahedron Lett 1997, 38, 8599; (i) Fujisawa, T.; Okumura, Y.; Morita, K.; Ukaji, Y. Bull Chem Soc Jpn 1992, 65, 3487; (j) Petasis, N. A.; Lu, S.-P. Tetrahedron Lett 1996, 37, 141; (k) Clark, J. S.; Kettle, J. G. Tetrahedron Lett 1997, 38, 123; (l) Clark, J. S.; Kettle, J. G. Tetrahedron 1999, 55, 8231; (m) Gravestock, M. B.; Knight, D. W.; Lovell, J. S.; Thornton, S. R. J Chem Soc, Perkin Trans 1 1999, 3143.
[168] (a) Katsumata, A.; Iwaki, T.; Fukumoto, K.; Ihara, M. Heterocycles 1997, 46, 605; (b) Hori, N.; Matsukura, H.; Matsuo, G.; Nakata, T. Tetrahedron Lett 1999, 40, 2811; (c) Lee, E.; Tae, J. S.; Chong, Y. H.; Park, Y. C. Tetrahedron Lett 1994, 35, 129.
[169] (a) Greeves, N.; Lee, W.-M. Tetrahedron Lett 1997, 38, 6449; (b) Greeves, N.; Lee, W.-M.; Barkley, J.

V. Tetrahedron Lett 1997, 38, 6453; (c) Nikolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C. K. J Am Chem Soc 1989, 111, 5330 and 5335; (d) Mori, Y.; Yaegashi, K.; Furukawa, H. J Am Chem Soc 1997, 119, 4557; (e) Trost, B. M.; Tenaglia, A. Tetrahedron Lett 1988, 29, 2927; (f) Suzuki, T.; Sato, O.; Hirama, M. Tetrahedron Lett 1990, 31, 4747; (g) Takagi, R.; Sasaoka, A.; Kojima, S.; Ohkata, K. Heterocycles 1997, 45, 2313; (h) Ramirez, M. A.; Padron, J. M.; Palazon, J. M.; Martin, V. S. J Org Chem 1997, 62, 4584; (i) Maezaki, N.; Matsumori, Y.; Shogaki, T.; Soejima, M.; Osishi, H.; Tanaka, T.; Iwata, C. Tetrahedron 1998, 54, 13087; (j) Arista, L.; Gruttadauria, M.; Noto, R. Heterocycles 1998, 48, 1325; (k) Martin, V. S.; Nunez, M. T.; Ramirez, M. A.; Soler, M. A. Tetrahedron Lett 1990, 31, 763.

[170] Arai, N.; Narasaka, K. Chem Lett 1995, 987.

[171] Durand, A. C.; Rodriguez, J.; Dulcère, J.-P. Synlett 2000, 731.

[172] Nair, V.; Balagopal, L.; Sheeba, V.; Panicker, S. B.; Rath, N. P. Chem Commun 2001, 1682.

[173] Salicylaldehyde is a useful bifunctional structural unit for the synthesis of various O-heterocycles of chemical and biological significance (see Refs. 174–176).

[174] O'Callaghan, C. N.; McMurry, T. B. M. J Chem Res, Synop 1997, 78.

[175] (a) Svetlik, J.; Hanus, V.; Bella, J. Liebigs Ann Chem 1989, 91; (b) Svetlik, J.; Turecek, F.; Hanus, V. J Chem Soc, Perkin Trans 1 1988, 2053.

[176] Yadav, L. D. S.; Saigal, S.; Pal, D. R. J Chem Res, Synop 1998, 307.

[177] Yadav, L. D. S.; Singh, S.; Singh, A. Tetrahedron Lett 2002, 43, 8551.

[178] (a) Patel, M.; Ko, S. S.; McHugh, R. J. Jr.; Markwalder, J. A.; Srivastava, A. S.; Cordova, B. C.; Klabe, R. M.; Erikson-Viitanen, S.; Trainor, G. L.; Seitz, S. P. Bioorg Med Lett 1999, 9, 2805; (b) Patel, M.; McHugh, R. J. Jr.; Cordova, B. C.; Klabe, R. M.; Erikson-Viitanen, S.; Trainor, G. L.; Ko, S. S. Bioorg Med Lett 1999, 9, 3221.

[179] Waxman, L.; Darke, P. L. Antiviral Chem Chemother 2000, 11, 1.

[180] Klasek, A.; Koristek, K.; Polis, J.; Kosmrlj, J. Tetrahedron 2000, 56, 1551.

[181] Girgis, A. S. Pharmazie 2000, 426.

[182] Mindl, J.; Hrabik, O.; Sterba, V.; Kavalek, J. Czech Chem Commun 2000, 65, 1262.

[183] Brain, C. T.; Paul, J. M. Synlett 1999, 1642.

[184] Phillips, A. J.; Uto, Y.; Wipf, P.; Reno, M. J.; Williams, D. R. Org Lett 2000, 2, 1165.

[185] (a) McKillop, A.; Sanderson, W. R. Tetrahedron 1995, 51, 6145 and references cited therein; (b) Muzart, J. Synthesis 1995, 1325 and references cited therein; (c) McKillop, A.; Sanderson, W. R. J Chem Soc, Perkin Trans 1 2000, 471 and references cited therein.

[186] European Patent EP 0 400 429 A3, 1990.

[187] Kumbhare, R. M.; Chinchkhede, P. W.; Ingle, V. N. Asian J Chem 2000, 12, 501.

[188] Sabnis, R. W.; Rangnekar, D. W. J Heterocycl Chem 1992, 29, 65.

[189] (a) Knölker, H.-J.; Wolpert, M. Tetrahedron Lett 1997, 38, 533; (b) Knölker, H.-J.; Fröhner, W. Synlett 1997, 1108.

[190] Turner, A. B. Synthetic Reagents; Pizey, J. S. (Ed.); Ellis Horwood: Chichester, UK, 1997; Vol. 3.

[191] Lemaire, M.; Guy, A.; Imbert, D.; Guetté, J. P. New J Chem 1991, 15, 379.

[192] Dell'Erba, C.; Novi, M.; Petrillo, G.; Stagnaro, P. J Heterocycl Chem 1994, 31, 861.

[193] Nishida, A.; Fuwa, M.; Naruto, S.; Sugano, Y.; Saito, H.; Nakagawa, M. Tetrahedron Lett 2000, 41, 4791.

[194] Dhiman, A. M.; Wadodkar, K. N.; Patil, S. D. Indian J Chem 2001, 40B, 636.

[195] Knight, D. W.; Little, P. B. J Chem Soc, Perkin Trans 1 2001, 1771.

[196] Kamitori, Y.; Hojo, M.; Masuda, R.; Fujitani, T.; Sukegawa, K. Heterocycles 1991, 32, 1693.

[197] Kamitori, Y.; Hojo, M.; Masuda, R.; Ohara, S.; Kawasaki, K.; Kawamura, Y. Synthesis 1990, 493.

[198] Kamitori, Y.; Hojo, M.; Masuda, R.; Fujitani, T.; Ohara, S.; Yokoyama, T. Synthesis 1988, 208.

[199] Kropf, H.; Reichwaldt, R. J Chem Res, Synop 1992, 130 and references cited therein.

[200] Walba, D. M.; Przybyla, C. A.; Walker, C. B. J Am Chem Soc 1990, 112, 5624.

[201] Brown, R. C. D.; Keily, J. F. Angew Chem, Int Ed 2001, 40, 4496.

[202] Cecil, A. R. L.; Brown, R. C. D. Org Lett 2002, 4, 3715.

[203] (a) Béres, M.; Hajós, G.; Riedl, Z.; Timári, G.; Messmer, A.; Holly, S.; Schantl, J. G. Tetrahedron 1997, 53, 9393; (b) Béres, M.; Hajós, G.; Riedl, Z.; Timári, G.; Messmer, A. Monatsch Chem 1998, 129, 897.

[204] Neville, C. F.; Grundon, M. F.; Ramachandran, V. N.; Reisch, J. J Chem Soc, Perkin Trans 1 1991, 259.

[205] Aranjo, A. D.; Bacher, E.; Demnitz, F. W. J.; Santos, D. A. Heterocycles 1999, 51, 29.

[206] (a) Kawase, M.; Kitamura, T.; Kikugawa, Y. J Org Chem 1989, 54, 3394; (b) Romero, A. G.; Darlington, W. H.; McMillan, M. W. J Org Chem 1997, 62, 6582.

[207] Skarzewski, J.; Siedlecka, R. Org Prep Proc Int 1992, 24, 623 and references cited therein.

[208] McDonald, C. E.; Nice, L. E.; Shaw, A. W.; Nester, N. B. Tetrahedron Lett 1993, 34, 2741.

[209] (a) Boons, G.; Brown, D. S.; Clase, J. A.; Lennon, I. C.; Ley, S. V. Tetrahedron Lett 1994, 35, 319; (b) Goti, A.; Romani, M. Tetrahedron Lett 1994, 35, 6567; (c) Goti, A.; De Sarlo, F.; Romani, M. Tetrahedron Lett 1994, 35, 6571; (d) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. Synthesis 1994, 639.

[210] Abele, E.; Lukevics, E. Heterocycles 2000, 53, 2285 and references cited therein.

[211] Gasco, A. M.; Di Stilo, A.; Fruttero, R.; Saba, G.; Gasco, A.; Sabatino, P. Liebigs Ann Chem 1993, 441.

[212] Godovikova, T. J.; Rakitin, O. A.; Golova, S. P.; Vorchikova, S. A.; Khmelnitskii, L. I. Mendeleev Commun 1993, 209.

[213] Jedlovska, A.; Lesko, J. Synth Commun 1994, 24, 1879.

[214] Armani, V.; Dell'Erba, C.; Novi, M.; Petrillo, G.; Tavani, C. Tetrahedron 1997, 53, 1751.

[215] Sorba, G.; Ermondi, G.; Fruttero, R.; Galli, U.; Gasco, A. J Heterocycl Chem 1996, 33, 327.

[216] Kotali, A.; Papageorgiou, V. P. Org Prep Proc Int 1991, 595 and references cited therein.

[217] Crandall, J. K.; Batal, D. J.; Lin, F.; Reix, T.; Nadol, G. S.; Ng, R. A. Tetrahedron 1992, 48, 1427.

[218] Park, K. H.; Jun, K.; Shin, S. R.; Oh, S. W. Synth Commun 1999, 29, 583.
[219] Molina, P.; Vilaplana, M. J.; Pastor, A. Synlett 1992, 873.
[220] Van De Walter, R. W.; Pettus, T. R. R. Tetrahedron 2002, 58, 5367 and references cited therein.
[221] (a) Quadrelli, P.; Invernizzi, A. G.; Falzoni, M.; Caramella, P. Tetrahedron 1997, 53, 1787 and references cited therein; (b) Gothelf, K. V.; Jørgensen, K. A. Chem Rev 1998, 98, 863 and references cited therein; (c) Dell, C. P. J Chem Soc, Perkin Trans 1 1998, 3873 and references cited therein; (d) Kotyatkina, A. I.; Zhabinsky, V. N.; Khripach, V. A. Russ Chem Rev 2001, 70, 641 and references cited therein; (e) Litvinovskaya, R. P.; Khripach, V. A. Russ Chem Rev 2001, 70, 405 and references cited therein.
[222] Trend, R. M.; Ramtohul, Y. K.; Ferreira, E. M.; Stoltz, B. M. Angew Chem, Int Ed Engl 2003, 42, 2892.