FURANS AND HYDROXYMETHYLFURANS: SUSTAINABLE SOURCES OF MOLECULAR DIVERSITY

DOI: http://dx.medra.org/10.17374/targets.2023.26.456

Ana L. Cardoso, Susana M. M. Lopes, Terver J. Sase, Teresa M. V. D. Pinho e Melo
University of Coimbra, Coimbra Chemistry Centre-Institute of Molecular Sciences (CQC-IMS),
Department of Chemistry, 3004-535 Coimbra, Portugal
(e-mail: tmelo@ci.uc.pt)

***Abstract**. The most used as well as the recently developed ring-opening transformations of furans, namely the Achmatowicz and Piancatelli rearrangements, and metal- and acid-catalyzed reactions, were highlighted. These highly efficient and versatile methodologies provide a plethora of functionalized heterocycles illustrating the wide applicability of these biomass-derived chemicals.*

Contents

1. Introduction

In the last decades, a significant research effort has been focused on the development of sustainable and efficient synthetic routes for the synthesis of various value-added chemicals and fuels from carbohydrate-derived furanic platforms such as furfural (FF) and hydroxymethylfurfural (HMF), promoted by the global environmental crisis and the rapid depletion of non-renewable fossil reserves.[1-5] Furans are on the list of the “Top-10” biomass-derived platform chemicals and the most promising compounds for further transformations.[6,7] FF and HMF are produced by hydrolysis and dehydration processes from lignocellulosic biomass, the most abundant and available renewable resource in nature (Figure 1).[8,9] The presence of highly reactive multiple sites/functionalities in these valuable building blocks, such as the aldehyde group, the hydroxy group, and the aromatic furan ring enables them to successfully participate in a great variety of transformations leading to the synthesis of a wide range of other furan derivatives as well as to various high-value chemicals.

This chapter highlights recent advances in furan ring-opening reactions, namely the Achmatowicz and the Piancatelli rearrangements of 2-hydroxymethylfurans into six-membered rings and functionalized cyclopentenones, respectively. Additionally, several metal-catalyzed transformations and the corresponding reaction mechanisms will be discussed. The final section provides an outlook on the Butin reaction as an approach to various functionalized heterocycles starting from furans.

2. The Achmatowicz rearrangement

The Achmatowicz rearrangement is an oxidative ring expansion of 2-hydroxymethylfurans (HMFn) into six-membered rings containing an oxygen (Figure 2).[10-13] This rearrangement is one of the most important furan transformations because it converts biomass-derived hydroxymethylfurans into molecules with high chemical and biological interest, which are difficult to obtain otherwise. Dihydropyranones obtained from the Achmatowicz rearrangement are highly functionalized and suitable for subsequent transformations. Nowadays, many research groups apply the Achmatowicz rearrangement to chiral HMFn obtained from furan or furfural by enantioselective methods as a strategy to produce highly functionalized chiral dihydropyranones able to undergo further transformations, which have been the focus of several nice reviews.[10-12] Many of them, reviewed the use of the Achmatowicz rearrangement as a strategy for the synthesis of a plethora of carbohydrates, glycosides, natural products and bioactive molecules.[14-19] The aza-variant of the Achmatowicz rearrangement has also been explored and involves the synthesis of dihydropyridinones from furfurylamines (Figure 2).[20-22] The aza-Achmatowicz rearrangement is mostly used in combination with subsequent transformations in the synthesis of alkaloids,[23,24] polysubstituted piperidines,[25,26] and other molecules with biological interest.[27,28]

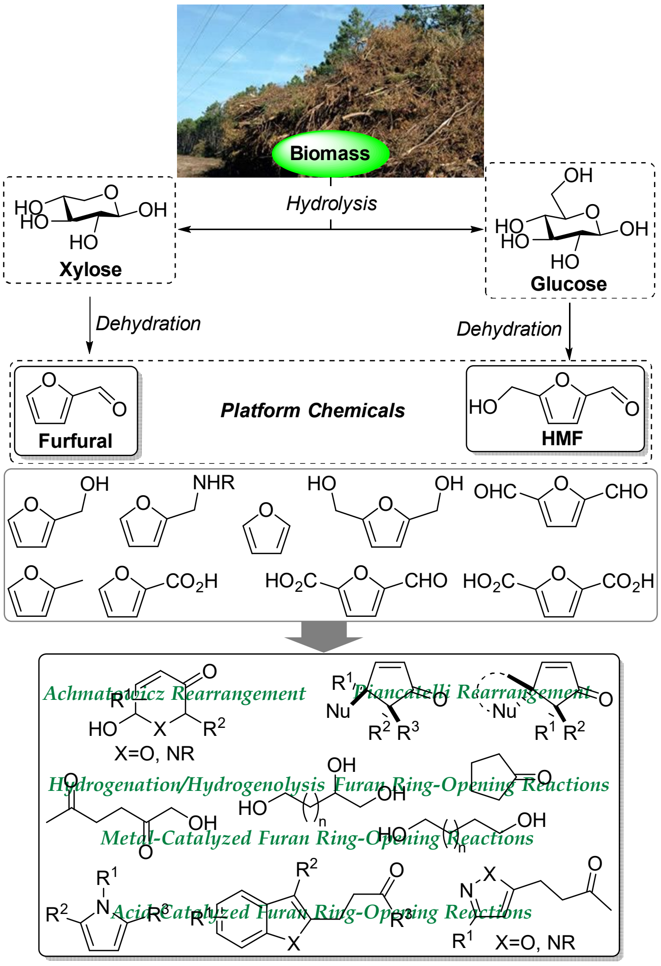


Figure 1. Biomass transformation into platform chemicals and subsequent reactions.

The increasing interest in the synthesis of dihydropyranones as possible precursors of other molecules with biological interest has made the Achmatowicz rearrangement a subject of study of several research groups. Although many procedures have been developed, in this chapter the most used and more recent developments in this field are described.

The first study on the conversion of HMFn into dihydropyranones dates back to 1971, and was reported by Achmatowicz and co-workers. This resulted from their work on the synthesis of monosaccharides from furans.[29] Prior to that, Clauson-Kaas and co-workers demonstrated that the oxidative bromination of furan gave 2,5-dimethoxydihydrofuran **1** using methanolic bromine at low temperature (Scheme 1a).[30] Inspired by the work of the Clauson-Kaas group, Achmatowicz and co-workers described the synthesis of dihydropyranones from HMFn, in a two-step approach (Scheme 1b).[29] Initially, HMFn were converted into dihydrofurans **2** by reaction with bromine in methanol. The process was efficient and gave dihydrofurans **2** in high yields as mixtures of *cis* and *trans* diastereoisomers. Hydrolysis of dihydrofurans **2**, in the presence of an acid, led to the furan ring-opening reaction to give acyclic dicarbonyl intermediate **I**, which underwent cyclization affording the thermodynamically favoured six-membered ring dihydropyranones. Although this transformation had been briefly mentioned by Cavill and co-workers during their studies on the synthesis of juvenile hormones,[31] Achmatowicz and co-workers extensively explored its applicability.

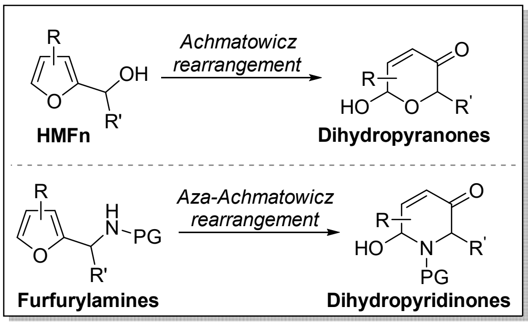
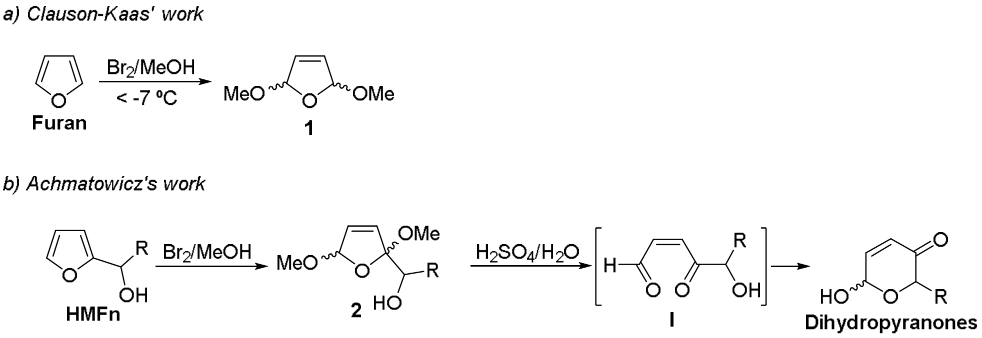


Figure 2. Classical Achmatowicz and aza-Achmatowicz rearrangements.

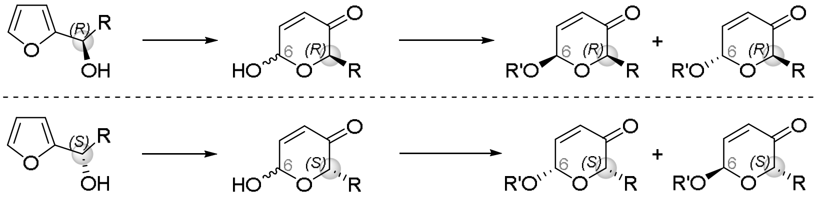


Scheme 1. a) Synthesis of 2,5-dimethoxydihydrofuran described by Clauson-Kaas and b) Achmatowicz rearrangement.

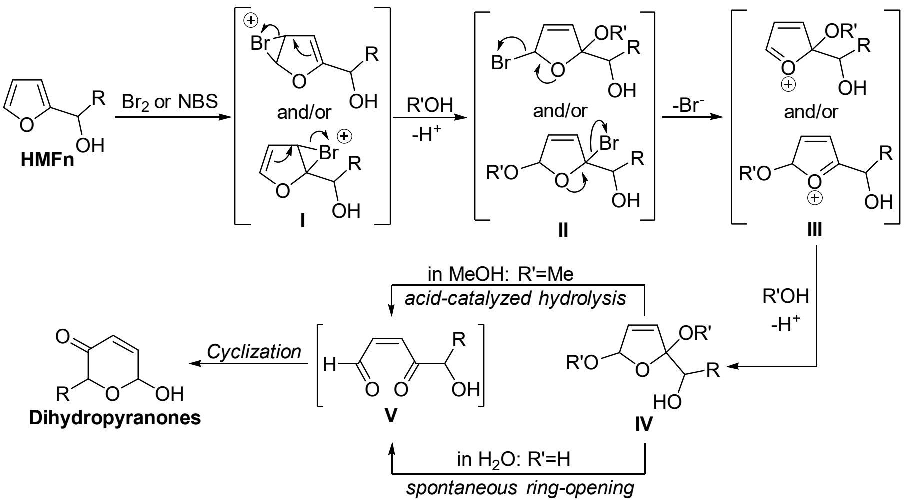
Initially, the Achmatowicz rearrangement was applied to the synthesis of several monosaccharides in racemic form.[29] However, some years later, Achmatowicz and co-workers demonstrated that it was possible to obtain enantiomerically pure saccharides starting from chiral HMFn, without loss of enantiomeric purity.[32,33] Thus, dihydropyranones with *R* or *S* configuration at C2 were obtained using HMFn with the same configuration at the exocyclic α-carbon. Although dihydropyranones were obtained as diastereoisomeric mixtures, they could be separated by chromatography or other techniques after further transformations, such as Pd-catalyzed glycosylation (Scheme 2).[34]

Since the first report, the Achmatowicz rearrangement has been the focus of several studies mainly aimed at using the suitable starting materials to obtain structural diversity, including chiral structures.

The Achmatowicz products, dihydropyranones, contain an additional oxygen atom with respect to their precursors (HMFn), therefore another reactant must be an oxygen source, such as water or alcohols. The systems Br_2/MeOH or H_2O and NBS/H_2O are the most used reactants to promote the Achmtowicz rearrangement.[10-12] The mechanism pathway is outlined in Scheme 3 for both reaction conditions. Initially, the oxidation of HMFn with molecular bromine in methanol yields the 2,5-dimethoxydihydrofurans **IV**, through the generation of bromonium ions **I**. The ring-opening of **I** by methanol gives intermediates **II**, which subsequently provides a *cis*/*trans*-mixture of isolable dihydrofurans **IV**, through intermediates **III**. The second step is the acid-catalyzed hydrolysis of dihydrofurans **IV** to give the acyclic intermediates **V**, which immediately undergo cyclization to the target dihydropyranones (Scheme 3, Br_2/MeOH or H_2O).[29,32,33,35] This methodology was improved by the use of *N*-bromosuccinimide (NBS) as bromine source and an aqueous solvent system.[36] In fact, the use of a mixture of THF/H_2O (4:1) as solvent, significantly improves the efficiency of the reaction since the ring-opening of dihydrofurans **IV** into the dicarbonyl compounds **V** is spontaneous avoiding the isolation of **IV** and the acid-catalyzed hydrolysis which is required when methanol is used as solvent (Scheme 3, NBS/H_2O).[36]



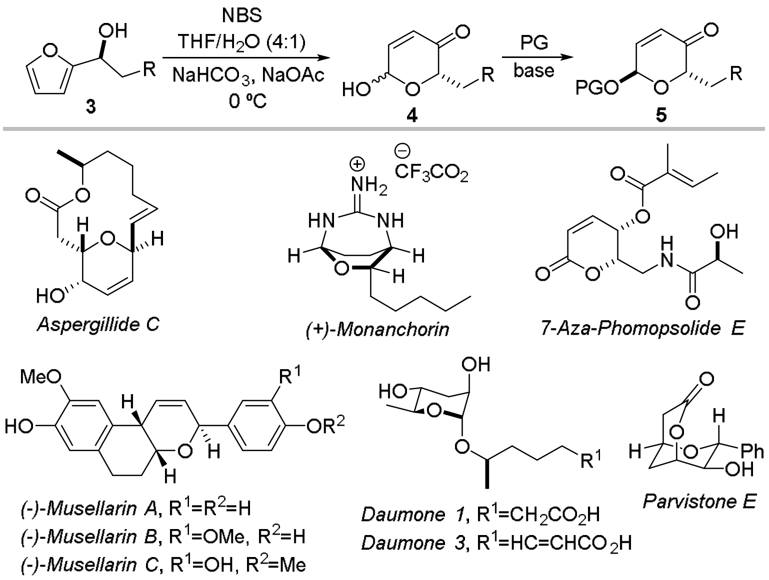
Scheme 2. Synthesis of enantiomerically pure compounds.



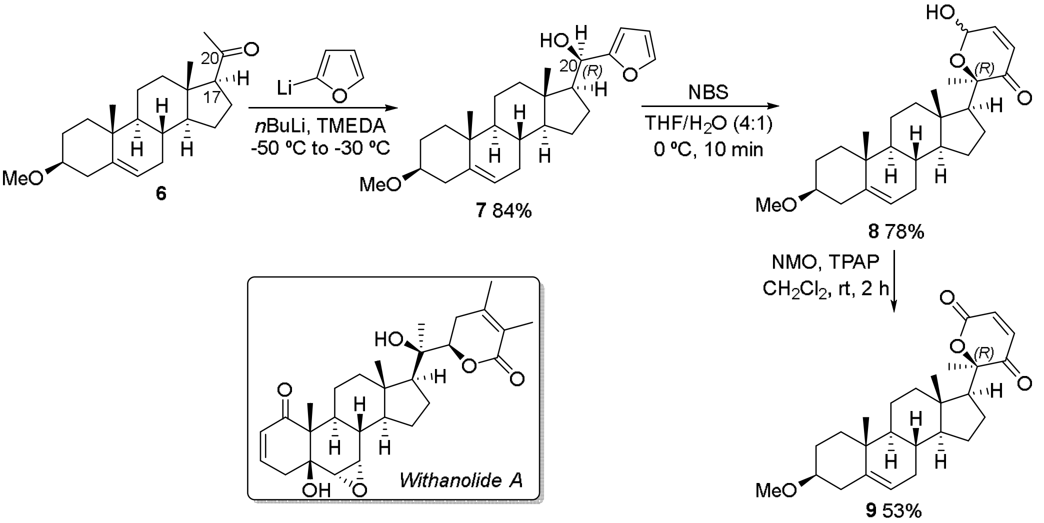
Scheme 3. Achmatowicz rearrangement by oxidative bromination in methanol and in water.

Many researchers have extensively studied the synthesis of a wide range of natural products in which the Achmatowicz rearrangement is a key step. Dihydropyranones **4** were prepared through the oxidative furan ring expansion of HMFn **3** using NBS as the bromine source in a THF/H_2O solvent system. During the reaction, hydrogen bromide is formed and $NaHCO_3$/NaOAc is used to buffer the reaction medium. The hydroxyl group of dihydropyranones **4** is often protected *in situ* to give **5**, in order to avoid degradations or undesired side-reactions. Natural products such as Monanchorin,[37] Daumone,[38] 7-aza-Phomopsolide E,[39] Aspergillide C[40,41] Musellarin A, B and C,[42] and Parvistone E[43] were prepared using the Achmatowicz rearrangement promoted by NBS/H_2O starting with nonracemic HMFn (Scheme 4).

Withanolide A is a natural steroid, containing a dihydropyran ring as side-chain at position C17, which exhibits neuroprotective properties against Alzheimer's diseases. Taylor and co-workers developed the synthesis of a pyrandione analogue **9** to mimic the Withanolide natural product using the Achmatowicz rearrangement as the key step (Scheme 5).[44] The addition of lithiated furan to C20 of 3β-methoxypregnenolone **6** gave the steroidal HMFn **7** diastereoselectively, which was transformed into the steroidal dihydropyranone **8** by the Achmatowicz rearrangement with NBS/H_2O in high yield and with retention of the configuration at C20. The oxidation of the Achmatowicz product gave pyrandione analogue **9**.

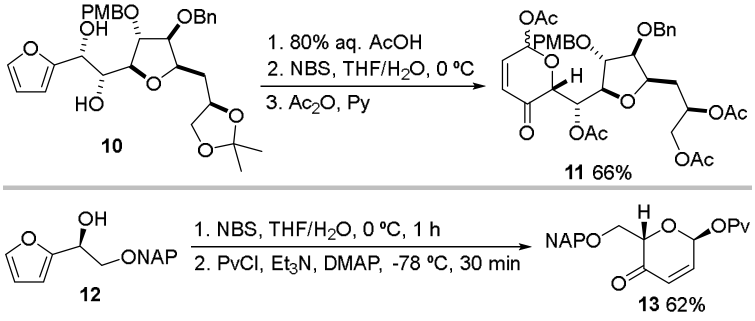


Scheme 4. Achmatowicz rearrangement using the NBS/H_2O procedure.



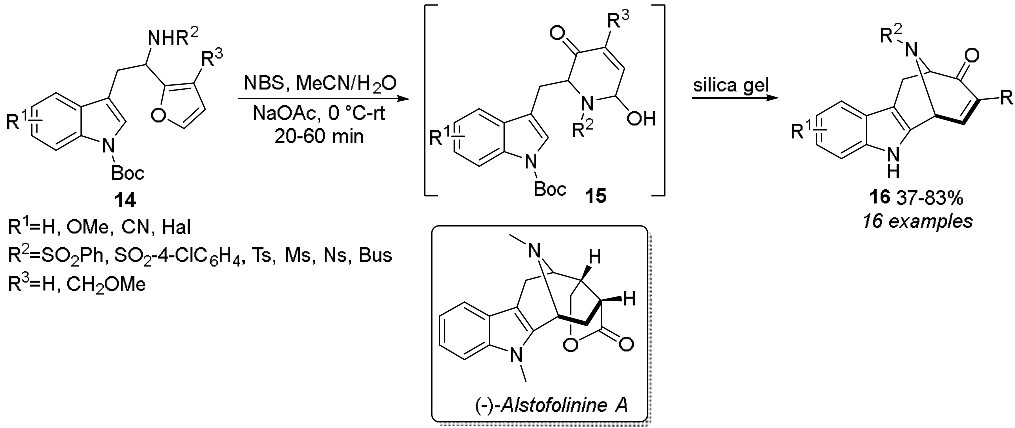
Scheme 5. Synthesis of Withanolide A analogue through Achmatowicz rearrangement.

Halichondrin B[45] and Maitotoxin[46] are two marine natural products that contain several fused dihydropyran rings and several chiral centers. The structure of Maitotoxin comprises 32 cyclic ether moieties of which 28 are pyran rings. One of the key strategies to obtain these complex structures is the Achmatowicz rearrangement for the construction of dihydropyran fragments, repeatedly employed for the construction of its complex structure. Dihydropyranone **11**, obtained from **10** *via* Achmatowicz rearrangement, is an intermediate in the synthesis of the fragment C1-C15 of Halichondrin B.[45] The conversion of HMFn **12** into dihydropyranone **13** is one example of the several transformations used in the total synthesis of Maitotoxin[46] (Scheme 6).



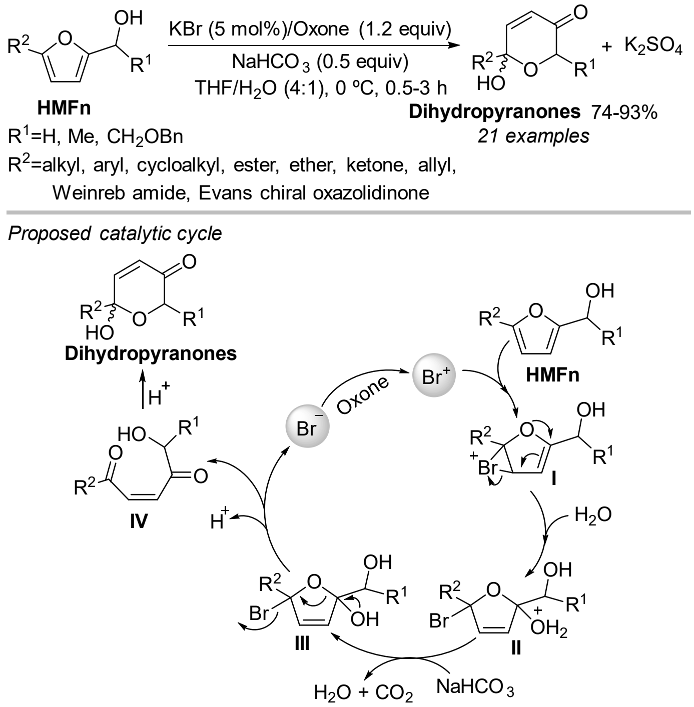
Scheme 6. Synthesis of intermediates of marine natural products.

Qi and co-workers explored the sequential aza-Achmatowicz rearrangement followed by an indole nucleophilic cyclization reaction to afford indole-fused azabicyclo[3.3.1]nonanes ring systems (Scheme 7).[47] Dihydropyridinones **15** were generated from furfurylamines **14** by the NBS-promoted aza-Achmatowicz rearrangement, which, upon treatment with silica gel in refluxing toluene, underwent cyclization reaction to give the target molecule **16** in high yields. This methodology was used in the total synthesis of the natural product Alstofolinine A.[47,48]



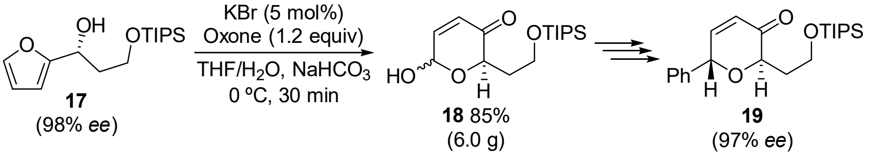
Scheme 7. Synthesis of indole-fused azabicyclo[3.3.1]nonanes through aza-Achmatowicz rearrangement.

In 2016, Tong and co-workers developed a catalytic environmentally friendly procedure for the Achmatowicz rearrangement using Oxone as terminal oxidant and KBr as catalyst.[49] Oxidation of KBr by Oxone™ generates an active transient brominating agent, which reacts with HMFn giving the bromonium ion **I**, thus triggering the Achmatowicz rearrangement similarly to NBS or Br_2 methods. The formation of acyclic intermediates **IV** and subsequent cyclization to dihydropyranones, releases bromide anion, which is oxidized again by Oxone for the subsequent catalytic cycle (Scheme 8). In this catalytic system the only side-product formed is the inorganic salt K_2SO_4, thus avoiding the formation of undesirable organic side-product observed in rearrangements promoted by *N*-bromosuccinimide (NBS) and the need for purification by flash column chromatography. In fact, the Achmatowicz products were purified by a simple liquid-liquid extraction and used in subsequent reactions without further purification. The KBr/Oxone methodology was applied to several HMFn derivatives giving better or competitive yields (74-93%) when compared with Br_2 or NBS methods. Moreover, a wide range of functional groups, such as silyl ether, ester, alkene, ketone, Weinreb amide, Evans chiral oxazolidinone and electron-rich arenes, remain unchanged using this catalytic system, without formation of by-products.



Scheme 8. Achmatowicz rearrangement using KBr/Ozone catalytic system.

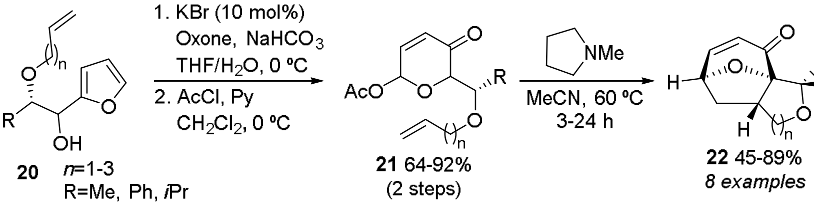
The scalability and the stereochemical integrity of the final product synthesized by this method were also evaluated (Scheme 9).[49] Dihydropyranone **18** was obtained in 85% yield on a 6.0 g scale from HMFn **17** by the catalytic KBr/Oxone Achmatowicz rearrangement and subsequent three-step functionalization of **18** provided the target compound **19** with high enantiomeric excess (*ee*).[49]



Scheme 9. Multigram Achmatowicz rearrangement in the synthesis of a dihydropyranone with high *ee*.

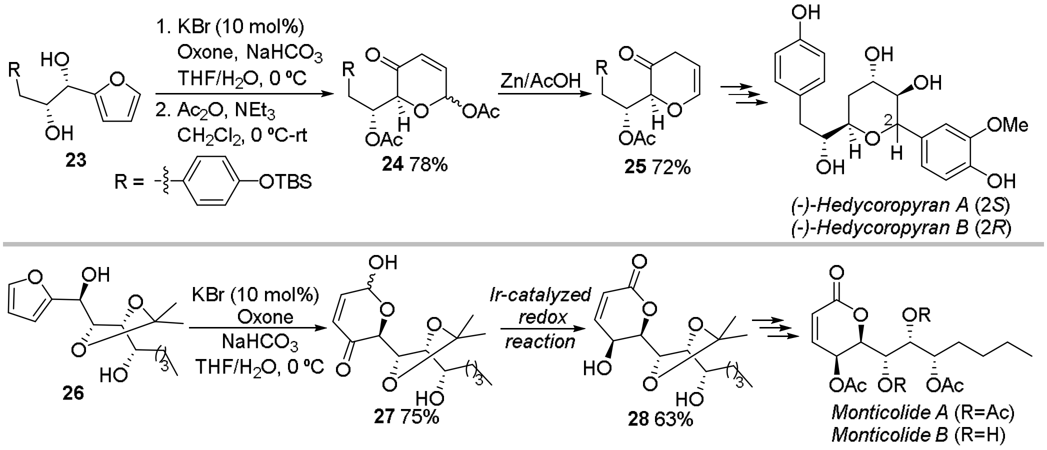
Gosh and co-workers developed the synthesis of a wide range of chiral 8-oxabicyclo[3.2.1]oct-3-enone ring systems through intramolecular [5+2]-cycloaddition of Achmatowicz rearrangement products (Scheme 10).[50] The Achmatowicz rearrangement of HMFn **20** with the catalytic system KBr/Oxone followed by the *in situ* hydroxyl group protection gave the dihydropyranones **21** in high yield (64-92%). Dihydropyranones **21** afforded enantiomerically pure 8-oxabicyclo[3.2.1]oct-3-enone products **22** through intramolecular diastereoselective [5+2]-cycloaddition.

The laboratory scalability, stereochemical integrity and absence of organic by-products of the Achmatowicz rearrangement with the KBr/Oxone catalytic system makes this methodology particularly interesting for the study of one-pot sequential reactions. Thus, this catalytic system has been employed in the preparation of key precursors in total synthesis of natural products.



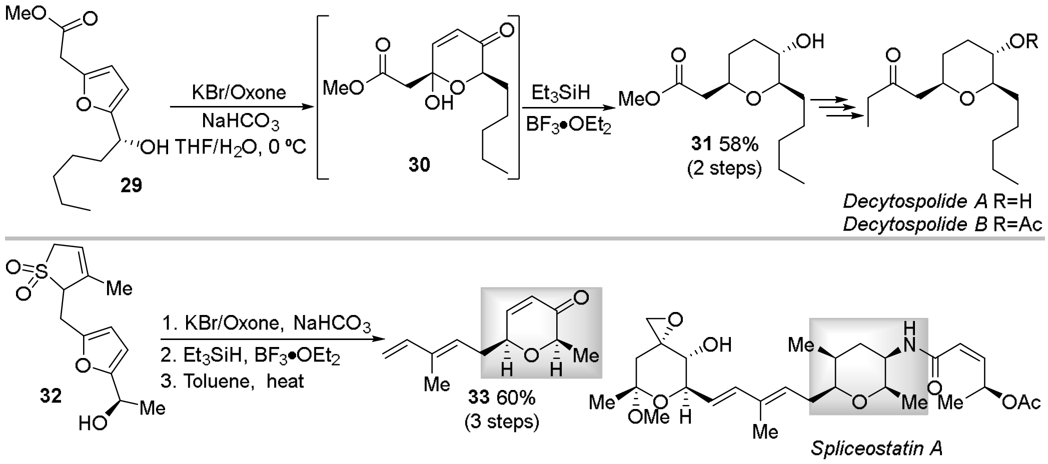
Scheme 10. Achmatowicz rearrangement on the synthesis of chiral 8-oxabicyclo[3.2.1]oct-3-enone ring systems.

Hedycoropyrans and Monticolides are natural products containing the tetra- and dihydropyran ring in their structure. The Achmatowicz rearrangement was the key step in the total synthesis of these compounds through the construction of the dihydropyranone ring (Scheme 11).[51,52] The Achmatowicz rearrangement of diols **23** and **26**, using the catalytic KBr/Oxone method, gave dihydropyranones **24** and **27**, respectively, in high yields. Dihydropyranones **24** and **27** underwent redox reactions giving enantiomerically pure intermediates **25** and **28**, which were further converted into the desired natural products.



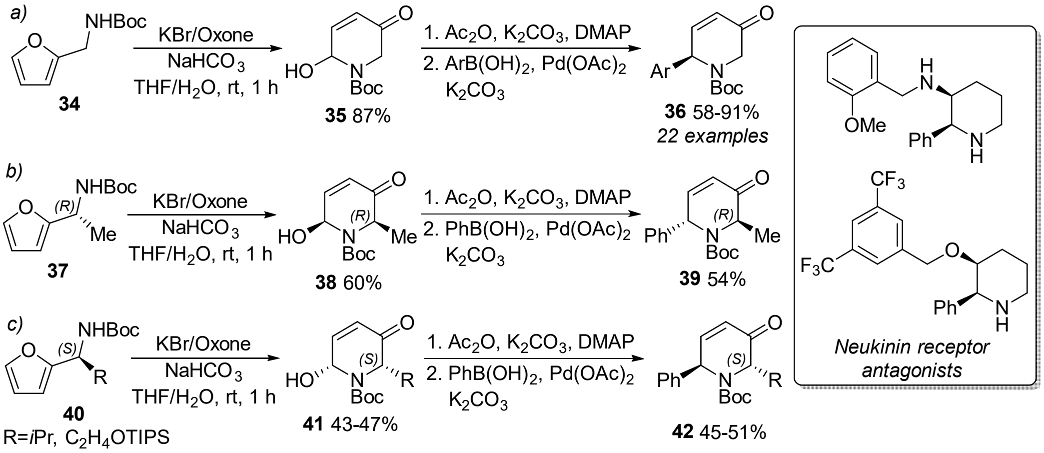
Scheme 11. Achmatowicz rearrangement in the synthesis of Hedycoropyrans and Monticolides.

The synthesis of tetrahydropyran **31**, a key intermediate in the synthesis of the natural products Decytospolide A and B, was obtained *via* sequential Achmatowicz rearrangement/Kishi reduction reaction in high yield (Scheme 12). Initially, the chiral HMFn **29** was subjected to the Achmatowicz rearrangement with KBr/Oxone allowing the formation of dihydropyranone **30**, followed by Kishi reduction giving the tetrahydropyran **31** as single diastereoisomer.[53] A similar approach was applied to HMFn **32** giving dihydropyranone **33** over a three-step procedure, comprising Achmatowicz rearrangement/Kishi reduction/deprotection reactions. Dihydropyranone **33**, a key fragment of bioactive molecules, was used in the synthesis of Spliceostatin A.[54]



Scheme 12. Key intermediates to the synthesis of Decytospolides and Spliceostatin A.

The aza-Achmatowicz rearrangement was also explored using the KBr/Oxone catalytic system as a strategy to obtain 2-aryldihydropyridinones which are valuable precursors of chiral 2-arylpiperidines and neukinin receptor antagonists (Scheme 13).[55]

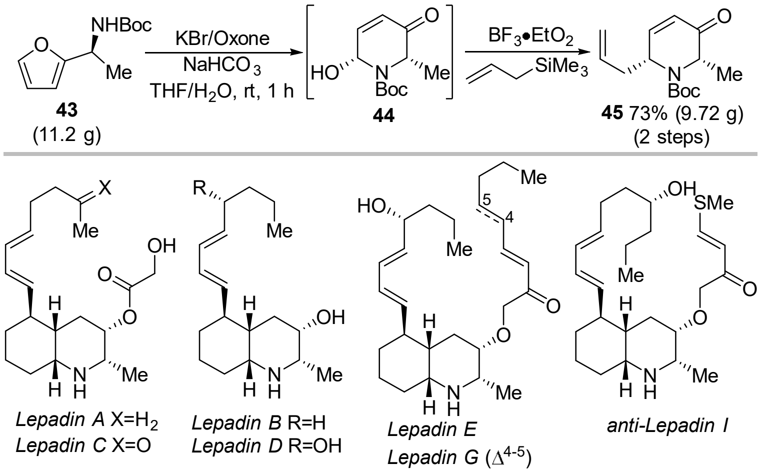


Scheme 13. KBr/Oxone-promoted aza-Achmatowicz of furfurylamines.

Dihydropyridinone **35** was obtained in high yield through the KBr/Oxone-promoted aza-Achmatowicz rearrangement of furfurylamine **34**, which was further converted into 2-aryldihydropyridinones **36** by hydroxyl group protection followed by Pd-catalyzed arylation with arylboronic acids. This methodology was applied to the efficient synthesis of various 2-aryldihydropyridinones, after kinetic resolution of aza-Achmatowicz rearrangement products (Scheme 13a). Moreover, the authors explored the KBr/Oxone-promoted aza-Achmatowicz rearrangement using enantiomerically pure furfurylamines (Scheme

13b and c). Thus, the aza-Achmatowicz rearrangement of furfurylamines **37** and **40** afforded 2,6-*cis*-dihydropyridinones **38** and **41**, respectively, in high yields. The subsequent Pd-catalyzed arylation gave 2-aryldihydropyridinones **39** and **42** as single stereoisomers with opposite absolute configuration.[55]

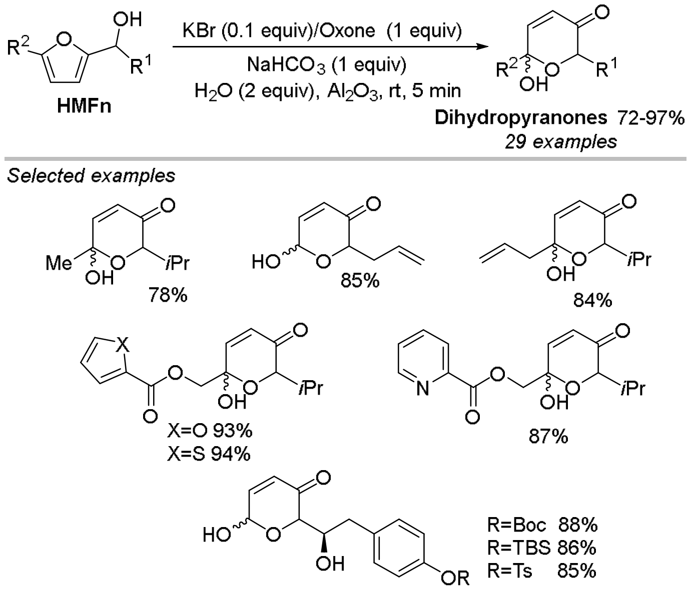
The KBr/Oxone-mediated aza-Achmatowicz rearrangement of chiral furfurylamine **43** allowed the generation of dihydropyridinone **44**, which was subjected to a diastereoselective allylation to give 2,6-*cis*-dihydropyridinone **45** in high yield. The synthesis of 2,6-*cis*-dihydropyridinone **45** could be carried out in a multigram scale (Scheme 14). 2,6-*cis*-Dihydropyridinone **45** was used as building block in the synthesis of Lepadin marine natural products.[56]



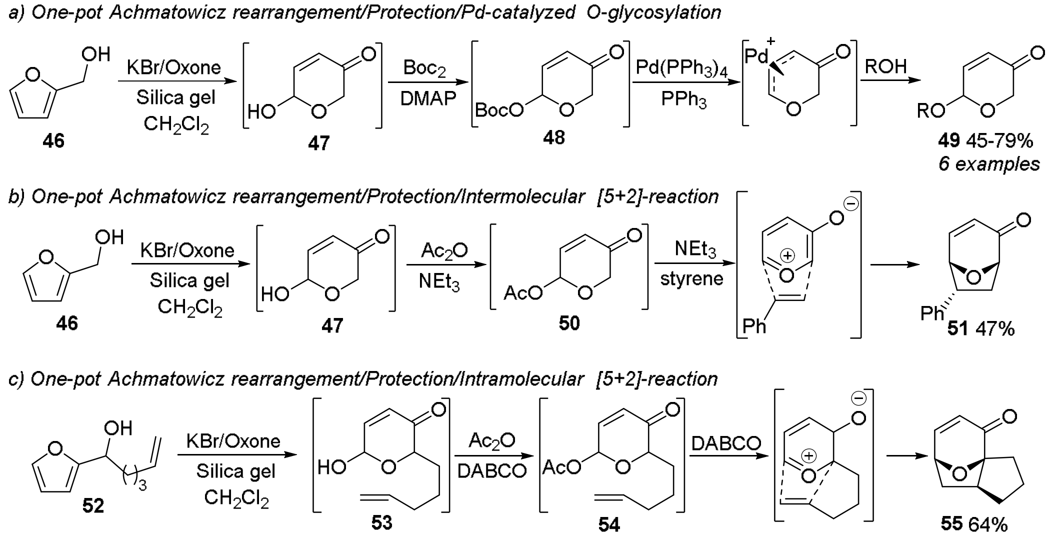
Scheme 14. Aza-Achmatowicz rearrangement for the synthesis of Lepadin marine natural products.

The use of the catalytic KBr/Oxone system in the Achmatowicz rearrangement has many interesting features. Besides being eco-friendly and efficient, the reaction tolerates a wide range of functional groups. However, the use of miscible THF/H_2O solvents is not ideal from a green chemistry point of view and can be undesirable for some one-pot Achmatowicz product functionalization. Thus, the research group of Tong developed a solvent-free version of the catalytic KBr/Oxone system using chromatographic alumina (Al_2O_3) as reaction medium.[57] HMFn suspended in Al_2O_3 were mixed and stirred with KBr (0.1 equiv), Oxone (1 equiv), H_2O (2 equiv) and $NaHCO_3$ (1 equiv) at room temperature for 5 min giving the corresponding dihydropyranones (Scheme 15). This solvent-free approach allowed a significant reduction of the reaction time (30 min using solvent vs 5 min under solvent-free conditions), and the products were isolated in high yields (72-97%) by simply washing the reaction medium with ethyl acetate. A wide range of functional groups were tolerated by this method, similar to what was observed using the THF/H_2O method. In addition, the Al_2O_3 could be reused at least 6 times without loss of efficiency and the reaction could be carried out in a multigram scale. The solvent-free protocol allowed performing sequential transformations of the Achmatowicz rearrangement products in a one-pot procedure, such as oxidation, *O*-acetylation, *O*-Boc protection, *O*-allylation, Kishi reduction and Ferrier allylation.

The same research group described the Achmatowicz rearrangement using silica gel and stoichiometric amounts of H_2O as oxygen source.[58] Under these conditions, it was possible to perform a one-pot three-step sequence contrary to other known methods. For example, the one-pot Achmatowicz rearrangement/protection/Pd-catalyzed *O*-glycosylation of HMFn **46** gave glycosides **49**, through intermediates **47** and **48**, without workup between the sequential steps in good overall yield (Scheme 16a). This study was also extended to the one-pot Achmatowicz rearrangement/acylation/intermolecular and intramolecular [5+2]-reactions to afford polycyclic systems **51** (*via* **47**→**50**) or **55** (*via* **52**→**53**→**54**) (Scheme 16b and c).[58]

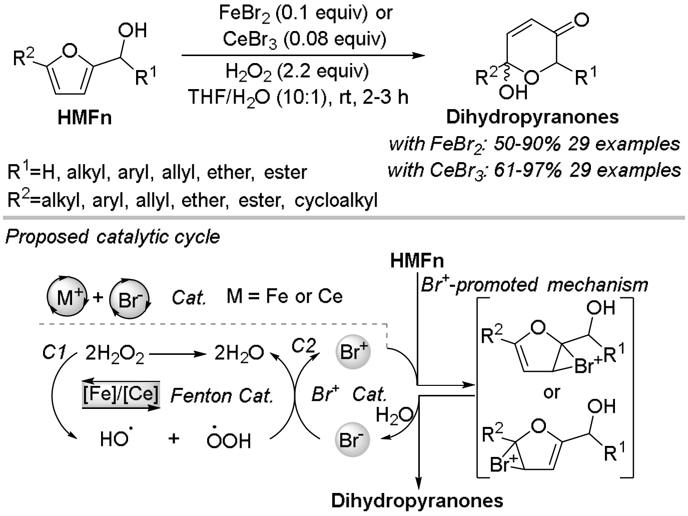


Scheme 15. Solvent-free Achmatowicz rearrangement.



Scheme 16. One-pot sequential Achmatowicz rearrangement/acylation/Pd-catalyzed *O*-glycosylation (a), intermolecular and intramolecular [5+2]-reactions (b and c).

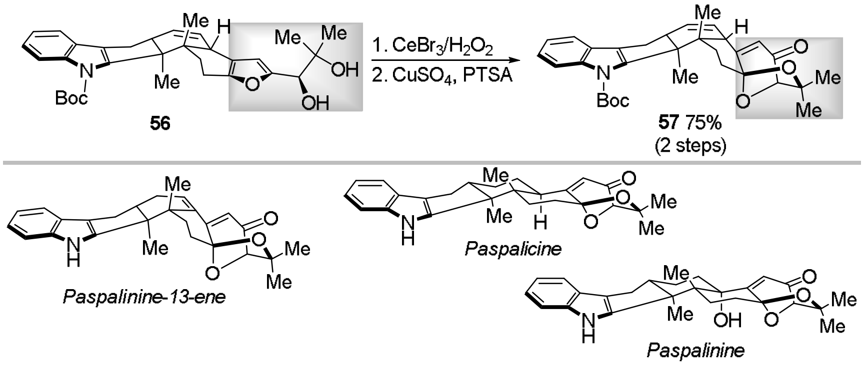
The development of new catalytic methods for Achmatowicz rearrangement is useful for finding more environmentally friendly synthetic methodologies.[59] In 2021, Tong and co-workers developed a new and greener methodology for the Achmatowicz rearrangement by exploring Fenton chemistry (Fe^{II}/H_2O_2) using a bifunctional catalyst ($FeBr_2$ or $CeBr_3$).[60] The mechanistic studies demonstrated that oxygen-based radicals ($HO^•$ and $HOO^•$) were generated from H_2O_2 by the Fenton catalyst (Fe^{II} or Ce^{III}) (*C1*, Scheme 17), and oxidized bromide to reactive brominating species (RBS, Br^+). HMFn were oxidized by the RBS, generated *in situ*, giving dihydropyranones *via* the formation of cyclic bromonium ion intermediates. Bromide anion was released in the process, similarly to what was observed when NBS or KBr/Oxone were used.[49] Bromide anion was reoxidized by the hydroxyl/hydroperoxyl radical generated *via* Fenton chemistry, entering the catalytic cycle again (*C2*, Scheme 17). Fenton chemistry and bromide redox worked in a synergetic way, with M-Br_x acting as a bifunctional catalyst.



Scheme 17. Fenton chemistry-promoted Achmatowicz rearrangement.

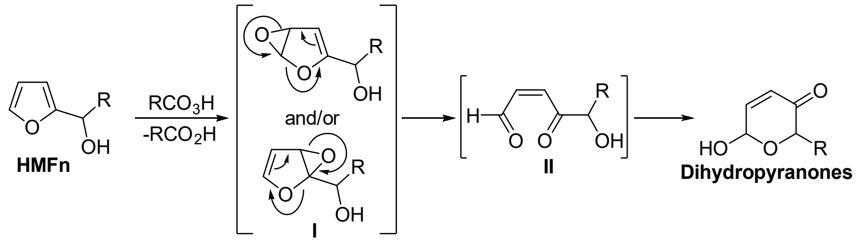
A wide range of dihydropyranones containing several functional groups were efficiently prepared by the Fenton chemistry-promoted Achmatowicz rearrangement of HMFn. $CeBr_3$ proved to be a more efficient catalyst (61-97% yield) than $FeBr_2$ (50-90% yield) under mild and neutral conditions. Moreover, four green chemistry metrics were used to evaluate the sustainability of this new procedure and they showed that it was much more efficient and environmentally friendly than the KBr/Oxone protocol.[49,60]

The $CeBr_3/H_2O_2$-promoted Achmatowicz rearrangement was recently applied in the total synthesis of indole diterpene natural products in a one-pot two-step procedure (Scheme 18).[61] Compound **57** synthesized by sequential Achmatowicz rearrangement/bicycloketalization of the HMFn **56** in 75% overall yield, is a key intermediate of the synthesis of heptacyclic Paspalicine, Paspalinine and Paspalinine-13-ene.



Scheme 18. Achmatowicz rearrangement/bicycloketalization in the synthesis of indole diterpenes.

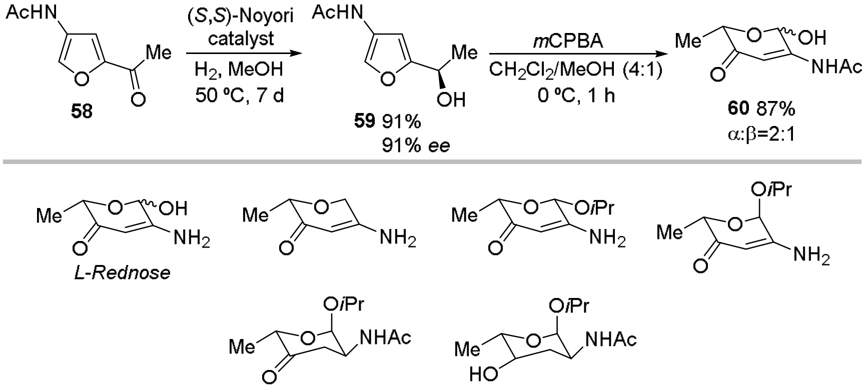
Almost at the same time as the Achmatowicz's first report, Lefebvre (in 1972) described a different procedure for the oxidative ring expansion of HMFn.[62] In that work, organic peracids, such as *m*-chloroperoxybenzoic acid (*m*CPBA) or peracetic acid, were used as oxidants in chlorinated solvents, leading to the efficient oxidative HMFn ring expansion.[62,63] The reaction mechanism starts with the epoxidation of HMFn resulting in the formation of epoxyalcohol intermediate **I**, which undergoes ring-opening to acyclic intermediate **II**. As in Achmatowicz's rearrangement, keto aldehyde intermediate **II** cyclizes to yield the dihydropyranone product (Scheme 19).



Scheme 19. Mechanism of the oxidative furan ring expansion using organic peracids.

The Achmatowicz rearrangement using peracids is well tolerated by a wide range of substrates under mild reaction conditions. This feature and the possibility to work in a multigram scale make this procedure a good alternative to bromide-induced methods for the total synthesis of natural and bioactive molecules.[14,17,64-66]

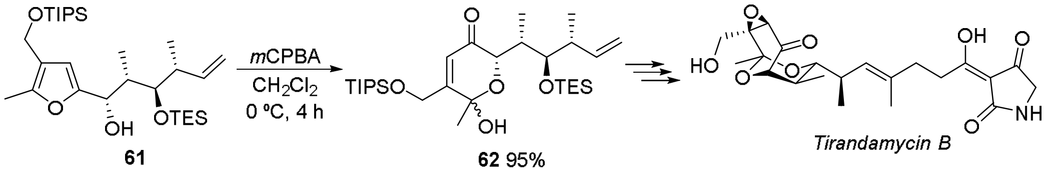
Sperry and co-workers applied the Achmatowicz rearrangement promoted by *m*CPBA in the synthesis of *L*-Rednose, a rare 2-amino sugar present in natural Anthracycline and Angucycline antibiotics, as well as in the synthesis of other 2-amino sugars (Scheme 20).[67] The synthesis of HMFn **59** was achieved by the asymmetric hydrogenation of ketone **58**, a chitin-derived compound obtained from the crustacean shell waste.[68] Oxidative ring expansion of HMFn **59** with *m*CPBA gave the dihydropyranone **60**, which proved to be a versatile intermediate in the synthesis of various 2-amino sugar derivatives, including *L*-Rednose (Scheme 20).[67]



Scheme 20. Synthesis of 2-amino sugars through Achmatowicz rearrangement.

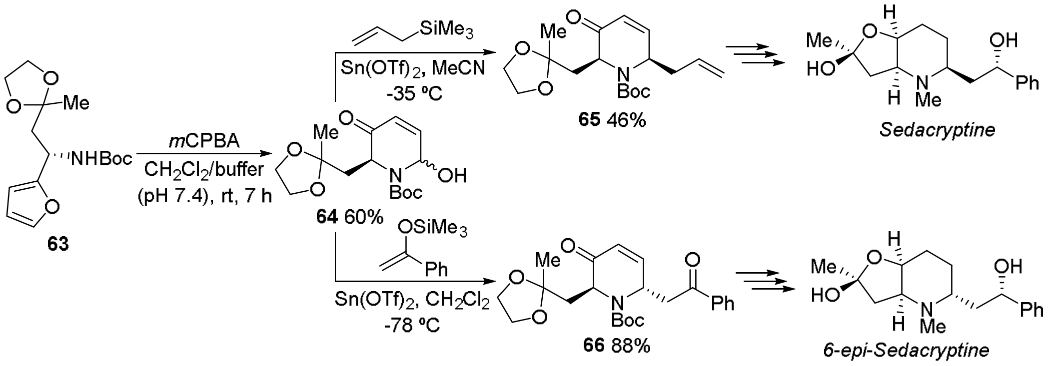
Tirandamycin B is a natural product isolated from *Streptomyces* species which have been studied as a promising lead scaffold for the treatment of lymphatic filariasis, a disease caused by the parasite *Brugia malavi*.[69] The importance of this natural product led Kato and co-workers to develop a synthetic strategy to Tirandamycin B (Scheme 21).[70] Thus, the authors subjected the multifunctionalized HMFn **61** to the

Achmatowicz rearrangement using *m*CPBA as oxidant to obtain the dihydropyranone **62** in high yield, keeping the integrity of the terminal alkene.



Scheme 21. Synthesis of Tirandamycin B *via m*CPBA-promoted Achmatowicz rearrangement.

The synthesis of Sedacryptine, an alkaloid isolated from *Sedum acre*, was accomplished using the *m*CPBA-promoted aza-Achmatowicz rearrangement as a key step (Scheme 22). The oxidative furan ring expansion of furfurylamine **63**, promoted by *m*CPBA, gave the dihydropyridinones **64** in high yield. The subsequent allylation with allyltrimethylsilane afforded the 2,6-*cis*-dihydropyridinone **65** as a single diastereoisomer, while the allylation with α-(trimethylsiloxy)styrene gave diastereoselectively 2,6-*trans*-dihydropyridinone **66**. This strategy was used in the total synthesis of Sedacryptine and its C6-*trans* epimer.[71]



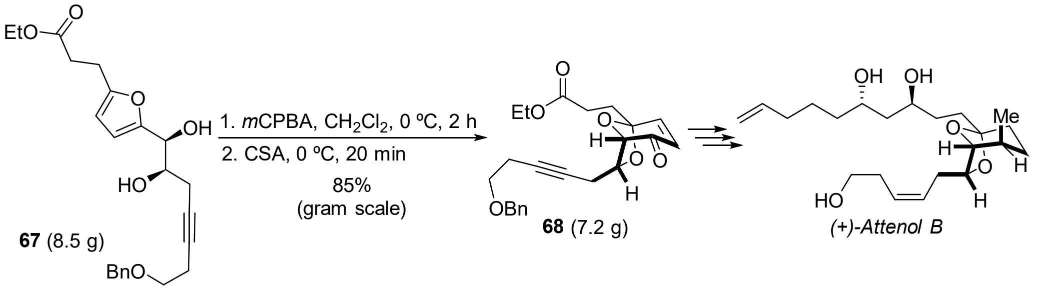
Scheme 22. Synthesis of Sedacryptine and its C6-*trans* epimer *via m*CPBA-aza-Achmatowicz rearrangement.

Many research groups have also used one-pot sequential reactions involving the *m*CPBA-promoted Achmatowicz rearrangement followed by *in situ* cyclization reactions as a strategy to obtain ring fused systems in the synthesis of natural products.

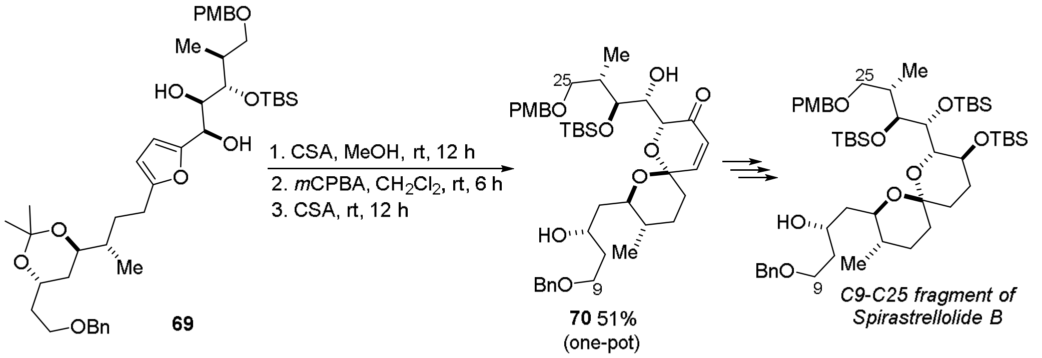
Tong and co-workers developed an efficient methodology for the total synthesis of Attenol B, a natural product isolated from Chinese bivalve *Pinma attenuate* which has demonstrated moderate cytotoxicity against P388 cell line. The key step of this strategy involves the Achmatowicz rearrangement of the HMFn **67**, using *m*CPBA as oxidant, followed by the *in situ* bicycloketalization through the addition of camphorsulfonic acid (CSA) to the reaction medium (Scheme 23).[72] Compound **68** was obtained in high yield in a multigram scale (7.2 g).

Similarly, Hanson and co-workers described a one-pot sequential deprotection/cascade Achmatowicz rearrangement-spiroketalization to produce the key spirocyclic intermediate **70**, essential in the synthesis of the C9-C25 fragment of Spirastrellolide B (Scheme 24).[73] The acetonide deprotection with CSA of HMFn **69** followed by treatment with *m*CPBA and finally the spirocyclization promoted by CSA, gave spirocyclic intermediate **70** in 51% yield over three reactions.

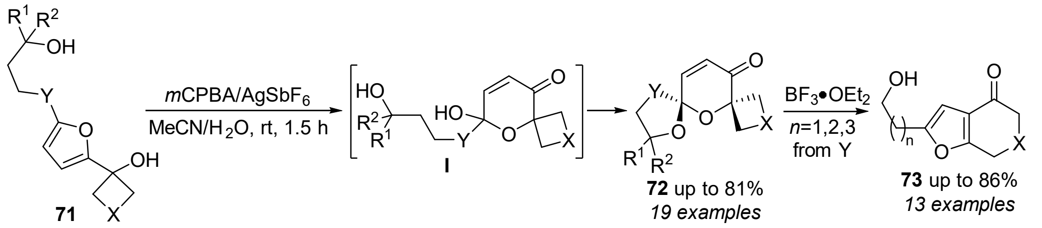
The oxidation of HMFn **71** with *m*CPBA in the presence of an additive ($AgSbF_6$) in a mixture of $MeCN/H_2O$ gave the dispiroacetals **72**, containing a four membered ring moiety, through Achmatowicz intermediates **I** (Scheme 25). Dispiroacetals **72** underwent an acid-catalyzed ring-opening/recyclization process to afford 6,7-dihydrobenzofuranones **73**, which can be used in further transformations.[74]



Scheme 23. One-pot Achmatowicz rearrangement/bicycloketalization in the total synthesis of Attenol B.



Scheme 24. Synthesis of key spirocyclic intermediate of C9-C25 fragment of Spirastrellolide B.



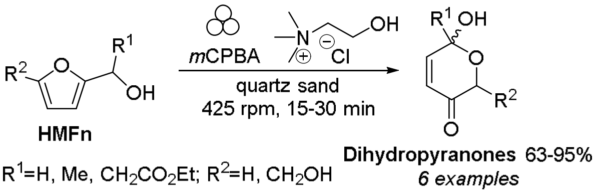
X=CH_2, CH(aryl), C(cycloalkyl), O; Y=CH_2, CHEt, $(CH_2)_2$, $(CH_2)_3$, CH_2O, CH(Et)O

R^1=H, Me, Ph; R^2=H, Me, Ph

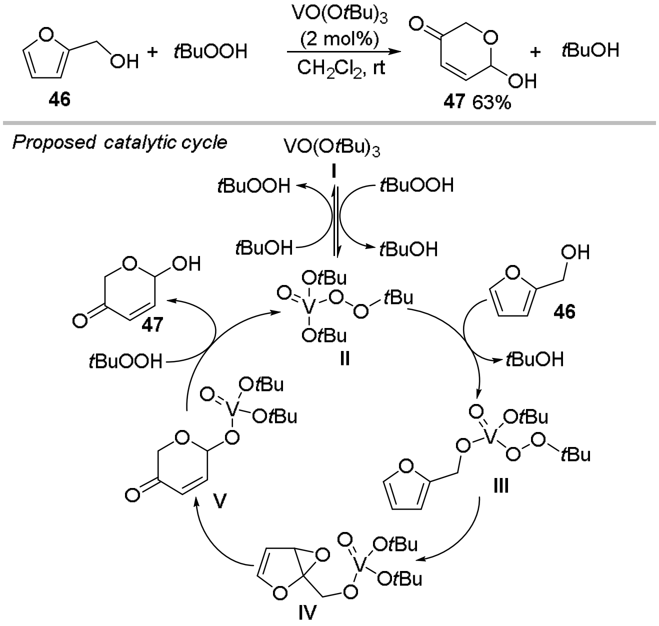
Scheme 25. Synthesis of dispiroacetals through tandem Achmatowicz rearrangement/acetalization.

Mechanochemistry has emerged as a powerful technique in organic synthesis for the sustainable synthesis of molecules with relevance in medicinal chemistry. The reduction of the energy consumed, the reduced amounts of solvents and organic waste are the major advantages of this methodology.[75] In 2015, König and co-workers described the first mechanochemical Achmatowicz conversion of HMFn into dihydropyranones promoted by *m*CPBA (Scheme 26).[76] The mechanochemically initiated Achmatowicz rearrangement was carried out in a planetary ball mill using quartz sand as solid support and choline chloride as additive, giving dihydropyranones in yields up to 95% in short reaction times.

tert-Butyl hydroperoxide (TBHP) is an oxidant capable of promoting the Achmatowicz rearrangement in anhydrous medium and in combination with catalytic amounts of a vanadium source allow the direct isolation of dihydropyranones or the direct use in subsequent transformations. This system was described for the first time by Ho and co-workers,[77] and later the mechanism involved was established by the Blackmond's research group, based on experimental and theoretical kinetic studies, as well as ^{51}V-NMR spectroscopic identification of catalytic species (Scheme 27).[78] Thus, the displacement of one alcohol molecule from the precatalyst specie **I** by TBHP provides the species **II**, which reacts with HMFn **46** to give the intermediate **III** and a second alcohol molecule. The intramolecular oxidation of complex **III** leading to epoxide **IV** is the rate-determining step which then rearranges to the complex intermediate **V**. Despite the assumption that rearrangement between intermediates **IV** and **V** occurs *via* 2,5-dihydrofuran intermediates, the exact mechanism involved was not explored. Dihydropyranone **47** was formed by action of another molecule of TBHP releasing the catalyst that re-enters the catalytic cycle.



Scheme 26. Synthesis of dihydropyranones using mechanochemistry.

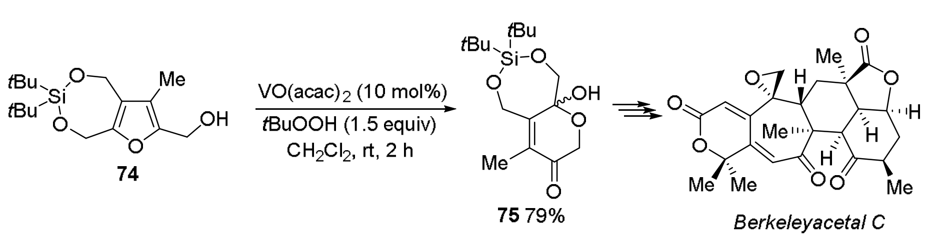


Scheme 27. Achmatowicz rearrangement with TBHP using VO(O*t*Bu)$_3$ as catalyst.

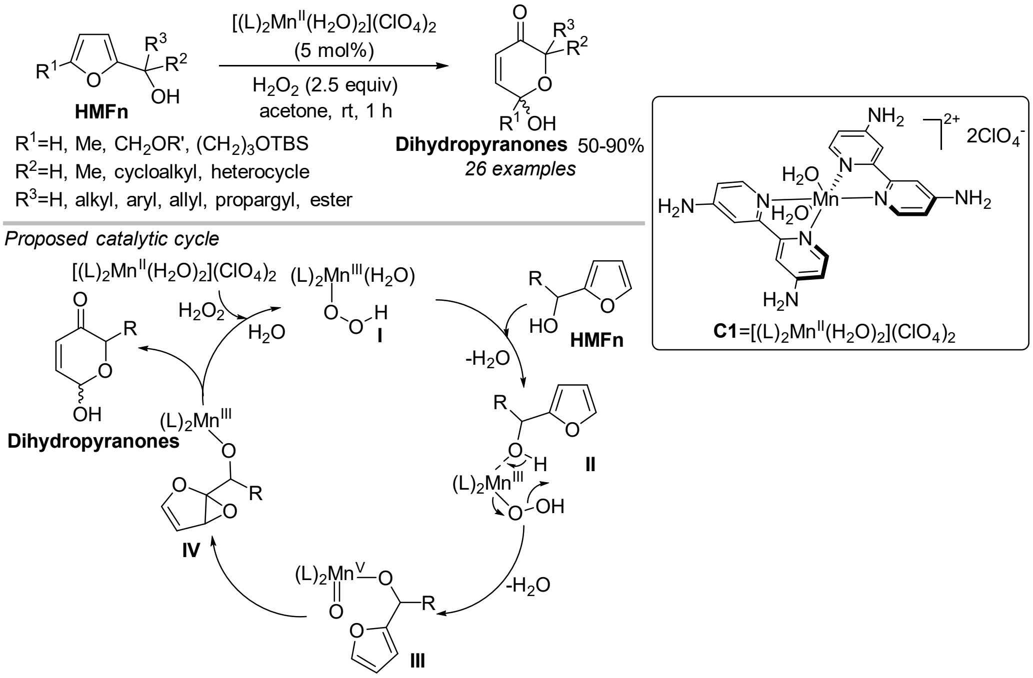
The catalytic system TBHP/VO(acac)$_2$ was successfully employed in the total synthesis of highly structurally complex compounds,[79,80] namely in the total synthesis of natural product Berkeleyacetal C (Scheme 28).[81] Dihydropyranone **75** was efficiently obtained (79%) from HMFn **74** using the vanadyl acetoacetonate as catalyst and TBHP as terminal oxidant, while other methods gave lower yields.

Manganese, the third most abundant transition metal in the earth's crust and characterized by a low toxicity, has been used in oxidation and epoxidation reactions.[82] In this context and considering the need to improve the sustainability of the Achmatowicz rearrangement, Yu and co-workers developed a Mn-catalyzed

HMFn oxidation strategy in combination with environmentally benign H_2O_2 as the terminal oxidant (Scheme 29).[83] Several catalytic systems were evaluated, and the stable Mn bipyridine pre-catalyst **C1** (5 mol%) using H_2O_2 (2.5 equiv) as terminal oxidant was the one that gave better yields of the Achmatowicz products (50-90%). The mechanistic cycle was initiated with the substitution of one H_2O molecule on the **C1** by H_2O_2 giving species **I**, which react with HMFn to form intermediates **II** releasing a second H_2O molecule. Highly reactive Mn^V-oxo intermediates **III** were generated by O-O bond cleavage and dehydration of intermediates **II**, which transfer an oxygen atom to the furan ring giving the epoxides **IV**. The release of Mn^{III} followed by furan ring-opening/hemiacetalation of **IV** gave the dihydropyranones. This strategy was successfully applied to the synthesis of several dihydropyranones, as well as piperidones *via* the aza-Achmatowicz rearrangement.[83]

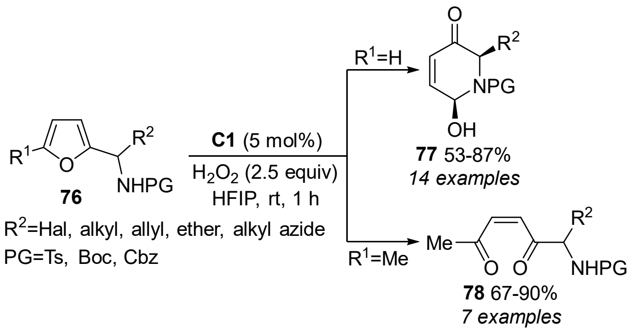


Scheme 28. Achmatowicz rearrangement in the synthesis of Berkeleyacetal C.



Scheme 29. Mechanistic cycle of the Mn-catalyzed Achmatowicz rearrangement.

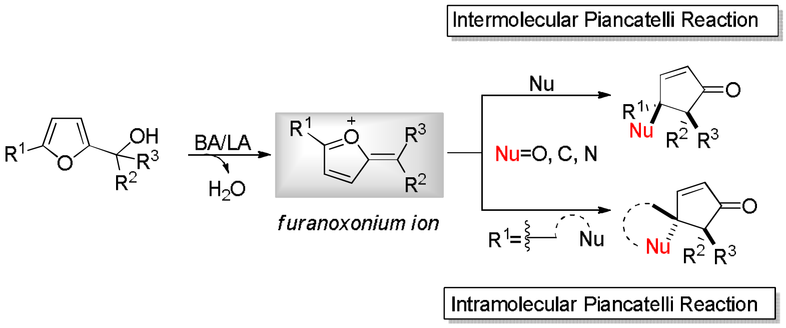
The Mn/H_2O_2 catalytic system was also employed in the aza-Achmatowicz rearrangement of furfurylamines (Scheme 30).[83] In fact, the oxidative furan ring expansion of 5-unsubstituted furfurylamines **76** (R^1=H) gave the corresponding dihydropyridinones **77** in high yields, with the *cis* isomer formed exclusively. However, the same reaction conditions applied to 5-substituted furfurylamines **76** (R^1=Me) afforded 1,4-diketoalkenes **78** as final products. This result demonstrated that the Mn/H_2O_2-promoted aza-Achmatowicz rearrangement is dependent on the steric hindrance of C5 position.



Scheme 30. Synthesis of dihydropyridinones and 1,4-diketoalkenes *via* Mn/H_2O_2-catalyzed oxidations.

3. The Piancatelli rearrangement

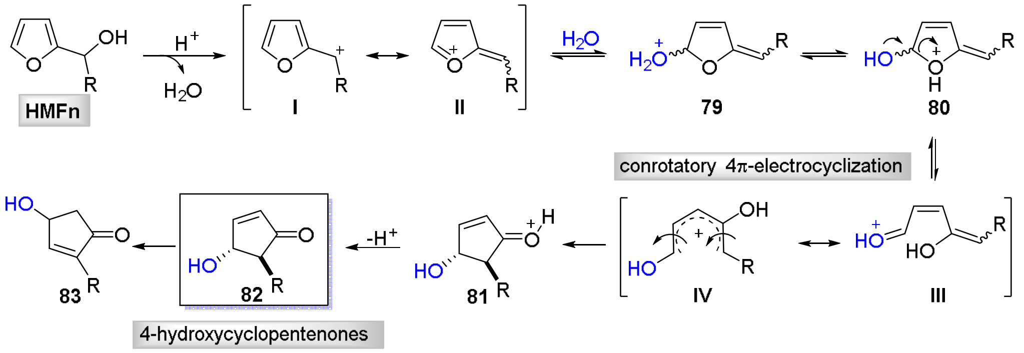
The Piancatelli reaction is a powerful method for accessing functionalized cyclopentenones from furfuryl alcohols by an acid-catalyzed rearrangement involving water as nucleophile. Initially reported in 1976, this transformation was only named as the Piancatelli reaction in 2004 and was primarily used in the synthesis of prostanglandin derivatives.[84-86] Since then, new variants of the Piancatelli reaction have emerged employing *C*- and *N*-nucleophiles as well as other furan precursors, broadening the scope of this reaction to target high added-value molecules (Scheme 31). Additionally, the increasing availability of biobased furanic platforms has also promoted the development of new synthetic strategies focused on biomass valorisation.[1,8,87,88] This topic was elegantly reviewed by Piutti[89] in 2013, and more recently by Popowycz[90] in 2018 and Cai[91] in 2022. In this section, selected examples on the classical Piancatelli rearrangement and its variants will be highlighted, including related cascade sequences and enantioselective transformations.



Scheme 31. Piancatelli reactions of furfuryl alcohols.

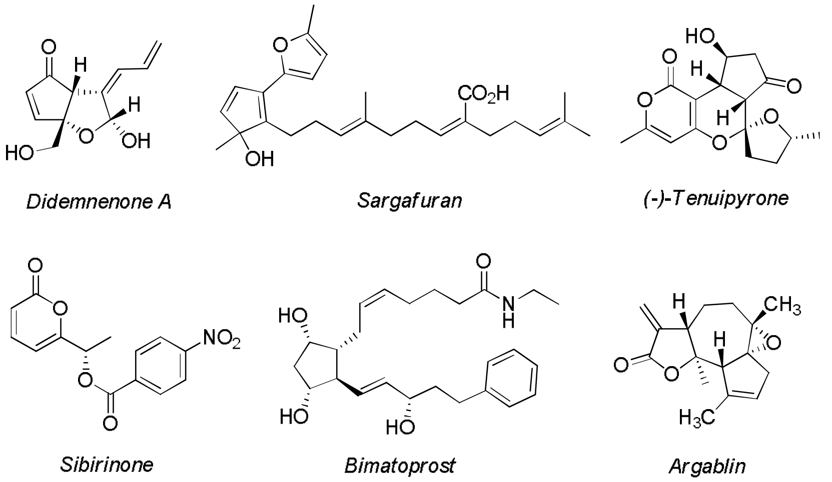
The classical approach has been explored for the transformation of HMFn into 4-hydroxycyclopentenones **82** under acidic aqueous conditions (Scheme 32). This transformation is triggered by the acid-mediated dehydration of the α-furylcarbinol to form a highly reactive furanoxonium intermediate **II**, which then reacts with water leading to **80**, in equilibrium with **79**, and undergoes furan ring-opening to generate pentadienyl cation **81**.[92] The final step involves a conrotatory 4π-electrocyclization to give diastereoselectively *trans*-4-hydroxy-5-substituted-cyclopent-2-enones **82**. Further isomerization into the thermodynamically more stable isomer **83** can also occur.[93] Theoretical calculations carried out by de Lera and co-workers support the pericyclic nature of the mechanism, with the high *trans* stereoselectivity resulting from the preferred *out,out*-geometry of the pentadienyl cation **IV**.[94] This mechanism is analogous to the

Nazarov cyclization, in which a divinylketone rearranges to a cyclopentenone, proceeding through a pentadienyl cation and a conrotatory ring-closure.[95]



Scheme 32. Proposed mechanism of the Piancatelli reaction.

4-Hydroxycyclopentenones are privileged scaffolds in organic synthesis that have been used to access a wide array of natural products and pharmacologically active compounds. Among the several methodologies available to build the 4-hydroxycyclopentenone motif, the Piancatelli reaction remains one of the most direct routes and has been extensively used as a key step in many synthetic sequences (Figure 3).[96-99]

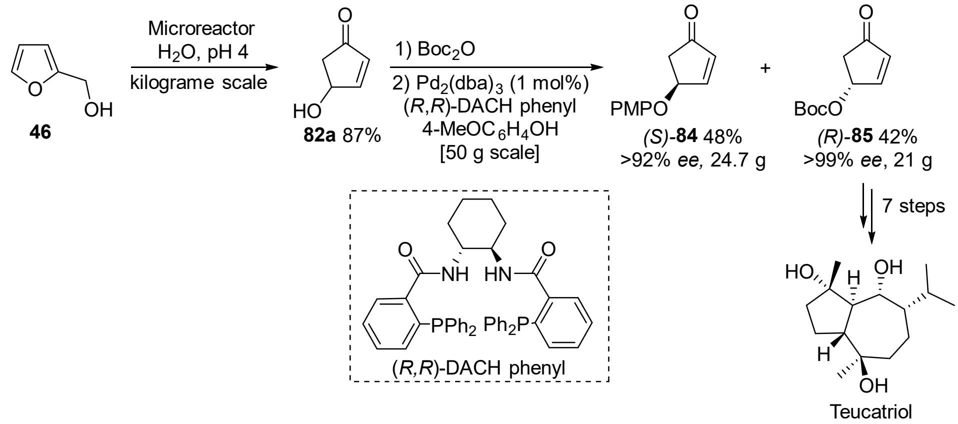

Didemnenone A *Sargafuran* *(-)-Tenuipyrone*

Sibirinone *Bimatoprost* *Argablin*

Figure 3. Natural and synthetic molecules prepared using the Piancatelli reaction as a key step.

4-Hydroxycyclopentenone **82a**, which is a common intermediate in the synthesis of Sibirinone[97] and (–)-Tenuipyrone,[98] can be easily accessed in kilogram scale from furfuryl alcohol **46** in acidic water in a reactor setup (Scheme 33).[100] Boc protection of **82a**, followed by resolution with *p*-methoxyphenol using Trost's technology furnishes pseudoenantiomeric building blocks (*S*)-**84** and (*R*)-**85** in multigram scale and high enantiopurity. These were found to be the ideal precursors for the synthesis of enantiopure substituted 2-cyclopentenones and the developed methodology was further applied to the synthesis of bioactive Teucatriol.

Despite the progresses made in the last two decades, in some cases the Piancatelli rearrangement still presents some drawbacks, namely the use of over- or stoichiometric amounts of Brønsted or Lewis acid to prevent side-reactions, moderate yields, or the formation of undesired polymeric material under the acidic reaction conditions which are difficult to remove.[99,101,102] Additionally, the rearrangement can lead to an inseparable mixture of 4-hydroxycyclopentenone isomers **82** and **83**, which usually require an additional step for the transformation into the thermodynamically more stable isomer **83** (see Scheme 32).



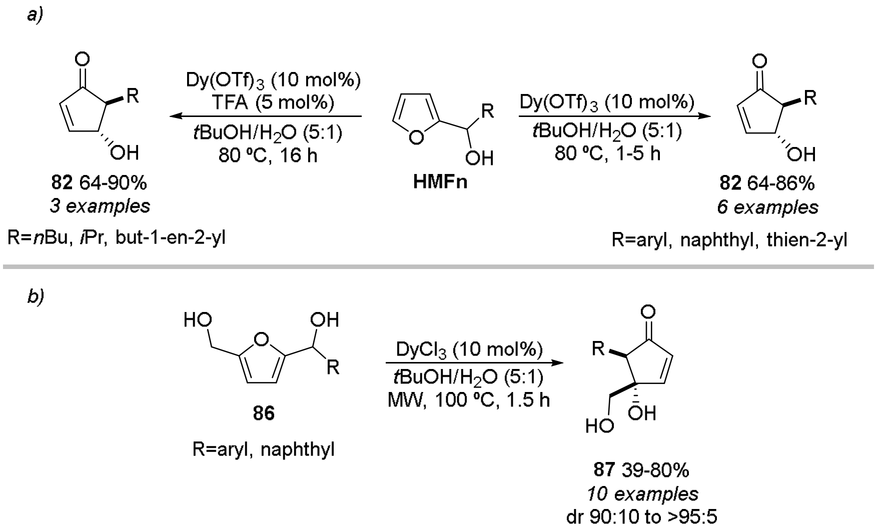
Scheme 33. Multigram synthesis of pseudoenantiomeric building blocks (*S*)-**84** and (*R*)-**85** using the Piancatelli reaction.

Representative reaction conditions for the Piancatelli rearrangement involve the use of dysprosium (III) salts as the catalyst (loading 5-10 mol%), under thermal conditions using conventional heating or microwave irradiation. In addition, the use of alcohols (*e.g.* *t*BuOH) as additives has been reported to increase the efficiency of the rearrangement. Furthermore, carrying out the reaction at high temperature (240 ºC) and pressure (1000 psi) in a microreactor significantly decreases the reaction time.[101,103]

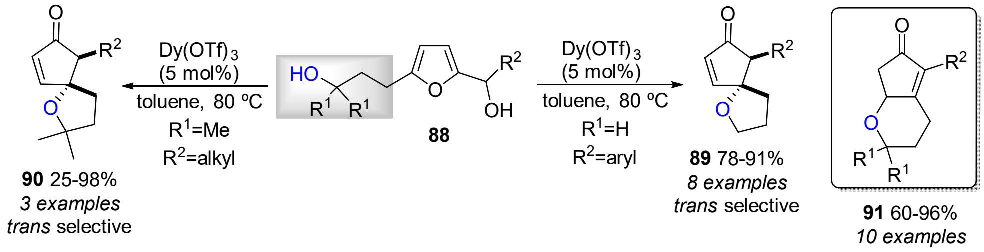
A highly efficient $Dy(OTf)_3$-catalyzed Piancatelli rearrangement of HMFn to single *trans*-4-hydroxycyclopentenones using a mixture of *t*BuOH/H_2O (5:1) as solvent has been disclosed (Scheme 34a).[104] Under the optimized reaction conditions at 80 ºC and using 10 mol% of $Dy(OTf)_3$, HMFn bearing an aryl group at the 2-position were smoothly converted into the corresponding *trans*-4-hydroxycyclopentenones **82** in good to high yields and short reaction time (1-5 h). The more challenging furylcarbinols with aliphatic side-chains, required a dual Lewis/Brønsted acid catalyst system of $Dy(OTf)_3$ (10 mol%) and TFA (5 mol%), and longer reaction time to afford the desirable cyclopentenones **82** in high yield.

More recently, the $DyCl_3$-catalyzed Piancatelli rearrangement of non-symmetrical furan-2,5-dicarbinols **86** under microwave irradiation originated 5-substituted-4-hydroxymethyl-4-hydroxycyclopentenones **87** in a regio- and diastereoselective fashion (Scheme 34b).[105] The rearrangement proceeded regioselectively in the more substituted carbinol moiety affording cyclopentenones **87** in yields ranging from 39% to 80%. However, the substrate scope of this method is limited to aryl substituents on **86** bearing both electron-withdrawing and electron-donating groups, since alkyl-derived furan-2,5-dicarbinols **86** fail to undergo the reaction.

The intramolecular oxa-Piancatelli rearrangement was established by Read de Alaniz's group using alcohols as nucleophiles and $Dy(OTf)_3$ as the catalyst, providing a novel synthetic route to oxaspirocycles in a highly diastereoselective manner (Scheme 35).[106] The cascade rearrangement process leads to the formation of the spirocyclic ether ring system and the tertiary stereocenter in a single step, generating the desired products **89** and **90** as single *trans* diastereoisomers in moderate to excellent yields. The substrate scope includes 2-aryl- and 2-alkyl-substituted furylcarbinols **88**, albeit the presence of substituent(s) on the alkyl chain, such as geminal dimethyl groups, is crucial for the 2-alkyl substituted furylcarbinols to undergo the rearrangement to the spirocyclic ethers **90**. The solvent choice also played a decisive role in the success of this transformation, since the use of solvents other than toluene led to decomposition of starting materials. Moreover, oxaspirocycles **89** and **90** could be efficiently converted into the more stable fused cyclopentenones **91** by treatment with Amberlyst®15 in heated toluene (Scheme 35).[107]



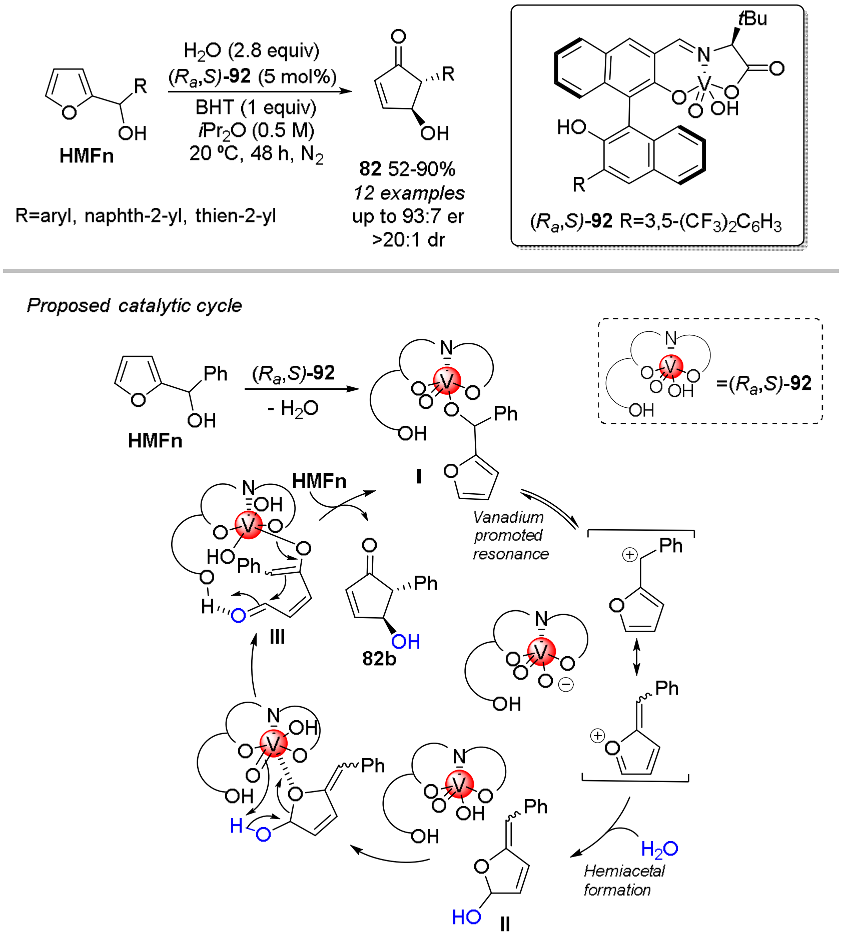
Scheme 34. Examples of the Lewis acid-catalyzed oxa-Piancatelli reaction.



Scheme 35. The intramolecular oxa-Piancatelli reaction.

The development of enantioselective oxa-Piancatelli reactions presented several challenges that only very recently were overcome. The use of water as a nucleophile has several drawbacks, namely its predisposition to decompose the reactants and catalysts in the reaction medium. Additionally, water is usually an inefficient nucleophile for many enantioselective transformations. Sasay and Gröger envisioned that a chiral oxovanadium complex could provide the water-resistant acid-catalytic system required for this transformation.[108] Within the several catalysts screened, the (R_a,S)-**92** bearing a 3,5-$(CF_3)_2C_6H_3$ group was the one that displayed higher catalytic activity, induced by the increased acidity of the phenolic hydroxy group and also by its bulkiness (Scheme 36). The optimized reaction conditions also involved the use of 3,5-di-*tert*-butyl-4-hydroxytoluene (BHT) as additive, due to its capacity of acting as antioxidant and preventing the decomposition of HMFn. Thus, the rearrangement of furylcarbinols carried out under the optimized reaction conditions, in the presence of 5 mol% of catalyst (R_a,S)-**92**, led to 4-hydroxycyclopentenone derivatives **82** in up to 90% yields and with 93:7 enantiomeric ratios. The proposed catalytic cycle is initiated by the reaction of the bifunctional vanadium catalyst with furylcarbinol under dehydration leading to intermediate **I**, followed by the generation and stabilization of the carbocation (Scheme 36). The addition of water at the furan C5 affords the corresponding hemiacetal **II**, which undergoes ring-opening assisted by its enolate bond to the Lewis acidic vanadium center giving rise to intermediate **III**.

This intermediate is converted into the target chiral product **82b** through an intramolecular aldol rearrangement.



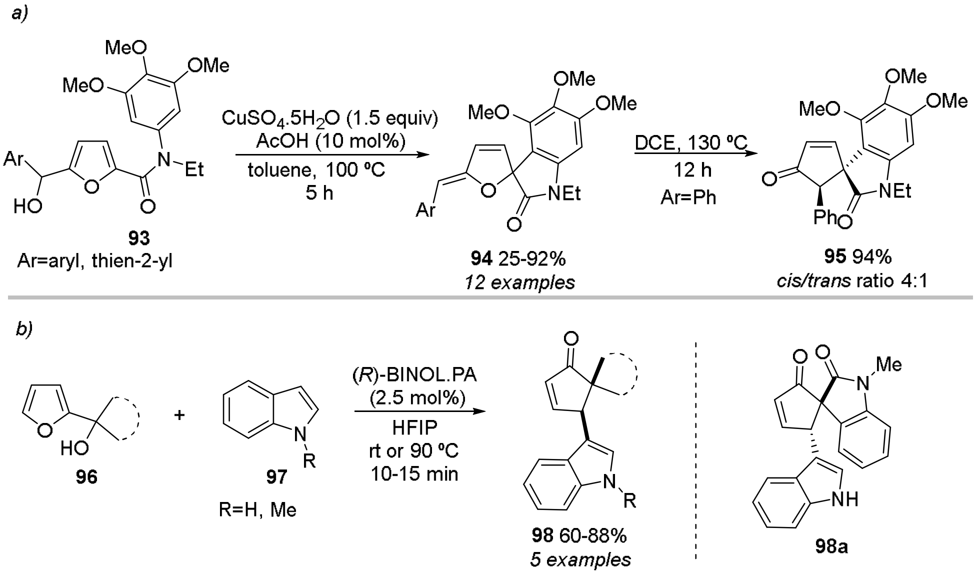
Scheme 36. The enantioselective catalytic oxa-Piancatelli reaction.

3.1. Carbo- and aza-Piancatelli reactions

In 2013, Yin and co-workers disclosed the first example of a stepwise C-Piancatelli rearrangement by using HMFn bearing an electron-rich *N*-aromatic ring that could act as an intramolecular nucleophile (Scheme 37a).[109,110] In the first step, a variety of hydroxybenzyl substituted furfurylamides **93** were efficiently converted into the corresponding spirofurooxindoles **94** in moderate to high yields through carbocyclization, under $CuSO_4{\cdot}5H_2O$/AcOH catalysis in toluene at 100 ºC. These spirocyclic compounds underwent further rearrangement in dichloroethane at 130 ºC to provide a mixture of *cis/trans* spiropentenoneoxindoles (*e.g.* **95**) through a 4π-electrocyclization process.

More recently, a highly efficient synthetic approach towards multifunctionalized spirocyclopentenones based on an intermolecular C-Piancatelly rearrangement under metal-free and mild reaction conditions, has been developed (Scheme 37b).[111] Tertiary HMFn **96** reacted smoothly with indoles **97** in hexafluoro-2-propanol (HFIP) in the presence of 2.5 mol% of (*R*)-BINOL-derived phosphoric acid

((*R*)-BINOL.PA) affording the corresponding indolyl spirocyclopentenone oxindoles **98** with short reaction time and high yield. This methodology was also successfully applied to *O*- and *N*-nucleophiles leading to a great variety of multifunctional spirocyclopentenones.



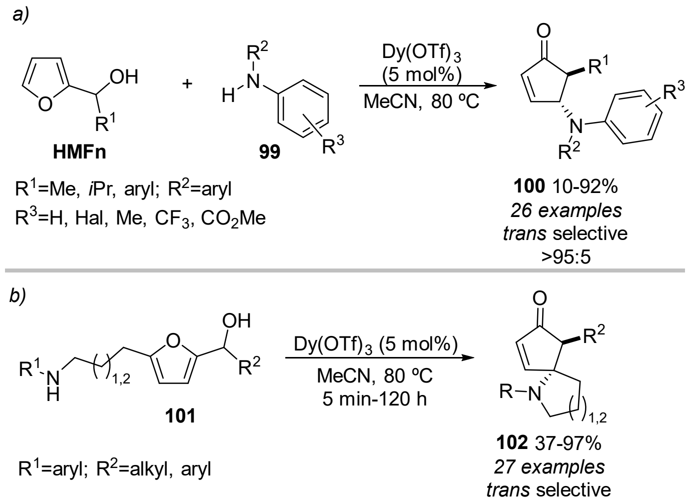
Scheme 37. Examples of the carbo-Piancatelli reaction.

Initially developed in 2010, the aza-Piancatelli reaction has become a powerful synthetic tool as demonstrated by the large number of publications on this topic in the last decade.[112] This straightforward strategy gives direct access to a large array of 4-aminocyclopentenones, a versatile building block for the synthesis of structurally diverse biologically active molecules and natural products.[113] The first report involved the $Dy(OTf)_3$-catalyzed reaction of secondary HMFn with anilines **99** in acetonitrile heated to reflux to give the corresponding 4-aminocyclopentenones **100** in yields ranging from 10 to 92% (Scheme 38a). One year later, the intramolecular version towards the synthesis of functionalized azaspirocycles **102** was successfully established by the same group using 2-furylcarbinols **101** bearing an 5-aminoalkyl side-chain as substrates (Scheme 38b).[114] The reaction proceeded diastereoselectively affording a great variety of azaspirocycles **102** as single *trans* diastereoisomers.

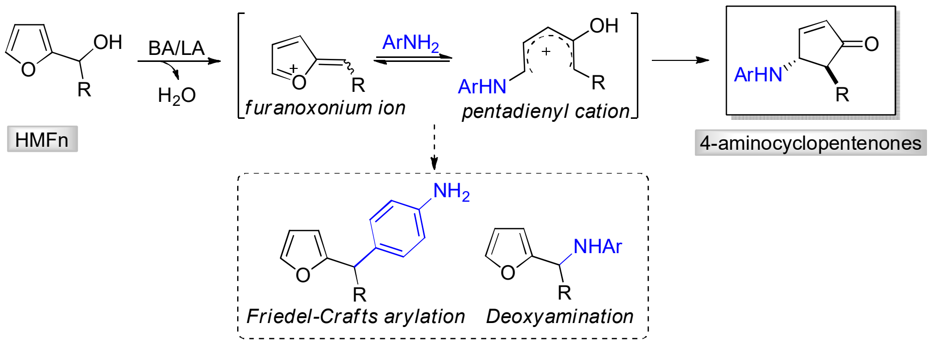
In the intermolecular reaction of HMFn with anilines, the furanoxonium ion generated through the acid-promoted dehydroxylation of HMFn reacts with the nitrogen nucleophile to generate a pentadienyl cation intermediate, which undergoes a 4π-electrocyclization providing 4-aminocyclopentenones in a diastereoselective fashion (Scheme 39). Along with the nucleophilic addition at the 2-position of the furanoxonium intermediate, other competitive side-reactions may occur leading to the formation of side-products resulting from Friedel-Crafts arylation and deoxyamination.

Mechanistic studies on the dysprosium triflate-catalyzed aza-Piancatelli rearrangement revealed the existence of a competitive binding between $Dy(OTf)_3$ and the aniline to form an inactive complex that limits the concentration of the available catalyst for triggering the rearrangement, having an impact on the reaction rate (Scheme 40).[115] This may also explain why weaker nucleophiles such as anilines are compatible substrates whereas more basic amines such as morpholine do not undergo the rearrangement under this catalytic system.

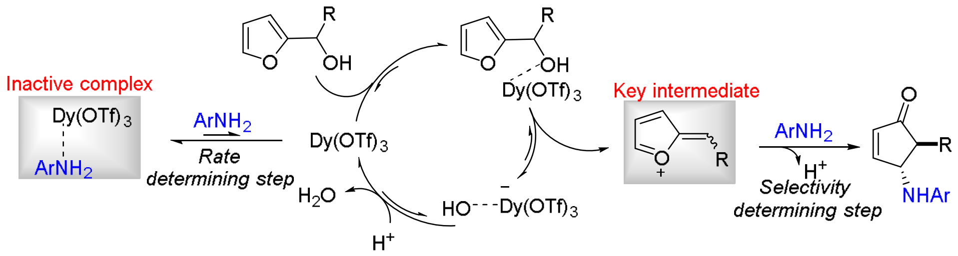
Over the years, several catalysts have been successfully employed to induce the aza-Piancatelli rearrangement, namely $Sc(OTf)_3$,[116] $In(OTf)_3$,[117] $Yb(OTf)_3$,[118] $AlCl_3$,[119] $BF_3{\cdot}Et_2O$,[119] $Ca(NTf_2)_2$,[120-124] and boronic acids.[125]



Scheme 38. First examples of the $Dy(OTf)_3$-catalyzed aza-Piancatelli reaction.

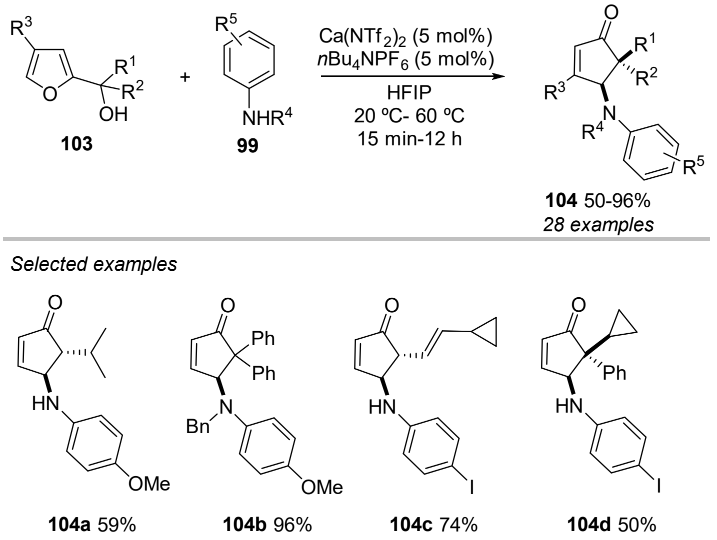


Scheme 39. The aza-Piancatelli reaction mechanism.



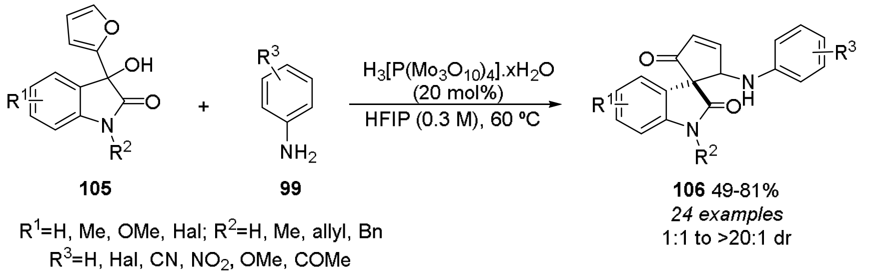
Scheme 40. Proposed mechanism for the $Dy(OTf)_3$-catalyzed aza-Piancatelli reaction.

Lebœuf and Gandon developed a highly efficient catalytic protocol which enables the aza-rearrangement to take place under mild reaction conditions, generally at room temperature, suitable for sensitive substrates (Scheme 41).[121] A series of HMFn **103** and substituted anilines **99** underwent the aza-Piancatelli cyclization in hexafluorisopropanol (HFIP) in the presence of $Ca(NTf_2)_2$ (5 mol%) and $n\mathrm{Bu}_6\mathrm{NPF}_6$ (5 mol%) to give the target products **104** in moderate to excellent yields. The method tolerates a wide scope of substituents on both reactants affording the 4-aminocyclopentenone derivatives **104** with high chemo- and stereoselectivity. The solvent HFIP showed higher selectivity than nitromethane, favouring the aza-Piancatelli reaction over Friedel-Crafts or deoxyamination reactions. Moreover, Lewis acidity studies and DFT calculations demonstrated that HFIP was acting as a Lewis acid and that its acidity was enhanced when combined with $Ca(NTf_2)_2$ and $n\text{Bu}_4\text{NPF}_6$ creating a synergistic effect.



Scheme 41. The aza-Piancatelli reaction catalyzed by HFIP, $Ca(NTf_2)_2$ and $n\text{Bu}_4\text{NPF}_6$.

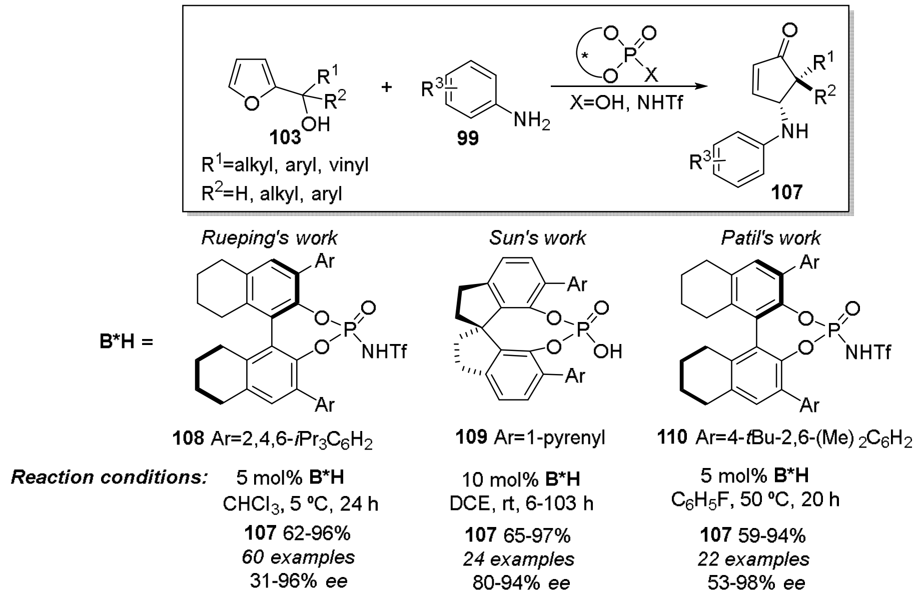
An array of functionalized spiroaminocyclopentenonyl oxindoles derivatives **106** have been recently prepared through the aza-Piancatelli rearrangement of 3-furanyl-oxindoles **105** in the presence of a variety of anilines, using phosphomolybdic acid and HFIP as catalytic system (Scheme 42).[126] The desired products were obtained in moderate to high yields, with anilines bearing electron-withdrawing groups providing better results over the electron-rich systems. Furthermore, furanyl-oxindoles **105** were also compatible substrates for the carbo-Piancatelli reaction with various indole derivatives, leading to the formation of spirocyclopentenonyl oxindole derivatives bearing an indole moiety with high degree of diastereoselectivity.



Scheme 42. The aza-Piancatelli reaction towards functionalized spirocyclopentenonyl oxindoles.

Optically active 4-aminocyclopentenones are highly desirable targets for synthetic chemists as direct precursors of a manifold of natural products and biologically active compounds. Despite being an attractive synthetic strategy towards these valuable building blocks, only a few examples of enantioselective aza-Piancatelli reactions have been reported, mainly due to the challenging task of achieving stereocontrol during the electrocyclization process.

The first examples were disclosed by Rueping,[127] Sun,[128] and Patil[129] who explored chiral phosphoric acids and phosphoramides as catalysts (Scheme 43). Rueping and co-workers carried out the reactions in chloroform at 5 °C for 24 h, using octahydro-BINOL-derived *N*-triflylphosphoramide **108** as catalyst. The mild protocol had a broad substrate scope giving access to a great variety of 4-aminocyclopentenones **107** in good yield and with excellent diastereo- and enantioselectivity. In the method developed by Sun's group the rearrangement was promoted by bis-pyrenyl-SPINOL-derived phosphoric acid **109** in dichloroethane at room temperature, giving the desired products in yields ranging from 65 to 97% with enantiomeric excess of 80-94%. The catalytic protocol reported by Patil and co-workers used diaryl-BINOL phosphoramide **110** in fluorobenzene at 50 °C for 20 h which led to chiral 4-aminocyclopentenones **107** in high yield and good to excellent enantioselectivity.



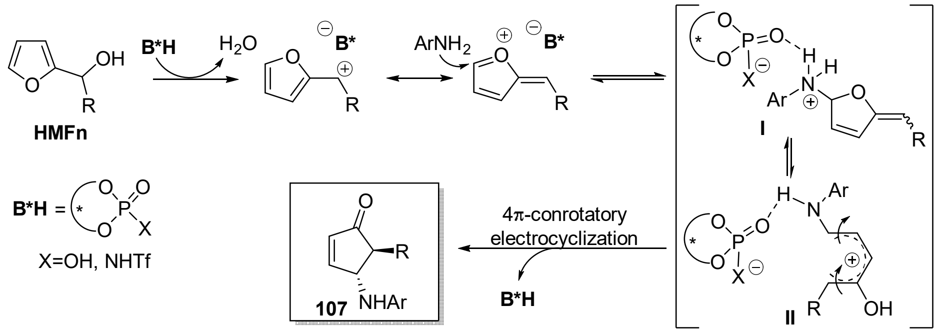
Scheme 43. The asymmetric aza-Piancatelli reaction catalyzed by chiral phosphoric acids and phosphoramides.

These methods explored the hydrogen-bonding sites in the key intermediates **I** and **II** to induce the enantiocontrol during the 4π-electrocyclization process, the step that determines both diastereo- and enantioselectivity of the rearrangement (Scheme 44).

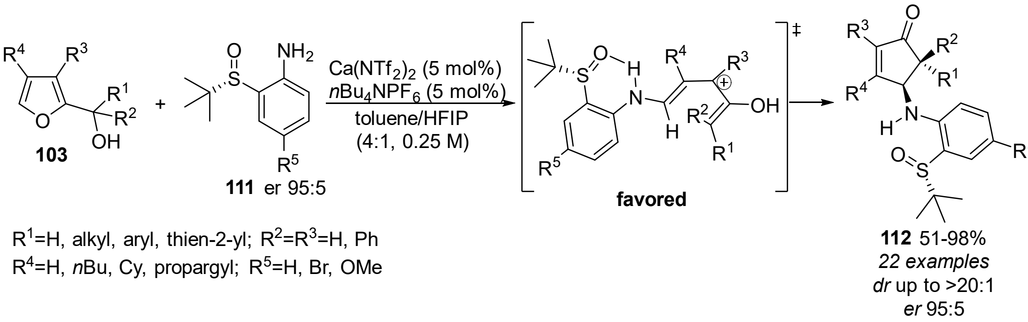
A different approach that uses enantiopure *o*-sulfinyl anilines as chiral auxiliaries, has been recently accomplished by Lebœuf and co-workers (Scheme 45).[130] This method combines their classical reaction conditions of $Ca(NTf_2)_2$ catalysis for promoting the dehydration step, with a chiral inducer (*e.g.* sulfoxide group) capable of forming a H-bond with the amine moiety and control the enantioselectivity of the electrocyclization. Under mild reaction conditions, a range of secondary and tertiary furfuryl alcohols **103** efficiently reacted with enantioenriched (*s*)-*o*-(*tert*-butylsulfinyl)anilines **111** to furnish the chiral 4-aminocyclopentenones **112** as the major diastereoisomer with up to 98% yield and 95:5 dr.

3.2. The Piancatelli rearrangement in cascade reactions

Catalytic domino reactions are becoming increasingly important in synthetic organic chemistry by providing atom- and step-economical methodologies for the construction of structurally complex frameworks starting from readily available precursors.[131] In the last decade, the Piancatelli rearrangement has been successfully incorporated in cascade and sequential reactions towards a variety of cyclic systems broadening the scope of its application in synthetic chemistry.[91]



Scheme 44. Proposed mechanism for the enantioselective aza-Piancatelli reaction catalyzed by chiral phosphoric acids and phosphoramides.

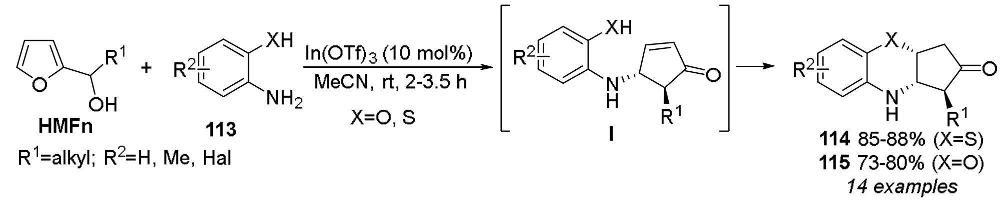


R^1=H, alkyl, aryl, thien-2-yl; R^2=R^3=H, Ph
R^4=H, *n*Bu, Cy, propargyl; R^5=H, Br, OMe

112 51-98%
22 examples
dr up to >20:1
er 95:5

Scheme 45. Stereoselective aza-Piancatelli reaction of 2-furylcarbinols with enantiopure *o*-sulfinyl anilines.

The first report involved a In(OTf)$_3$-catalyzed domino aza-Piancatelli/hetero-Michael addition for the synthesis of 3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine and thiazine derivatives developed by Subba Reddy's group.[132] A series of HMFn reacted smoothly with 2-aminothiophenols or 2-aminophenols **113** in the presence of 10 mol% of In(OTf)$_3$ in acetonitrile at room temperature to give the corresponding fused cyclopentenones **114** and **115**, respectively, in high yield (Scheme 46). In the same year, another group reported the same reaction sequence using La(OTf)$_3$ as catalyst. However, this method required harsher reaction conditions and was limited to 2-aminophenols and benzene-1,2-diamines as reaction partners, affording the desired products in lower yields and longer reaction times.[133]



R^1=alkyl; R^2=H, Me, Hal

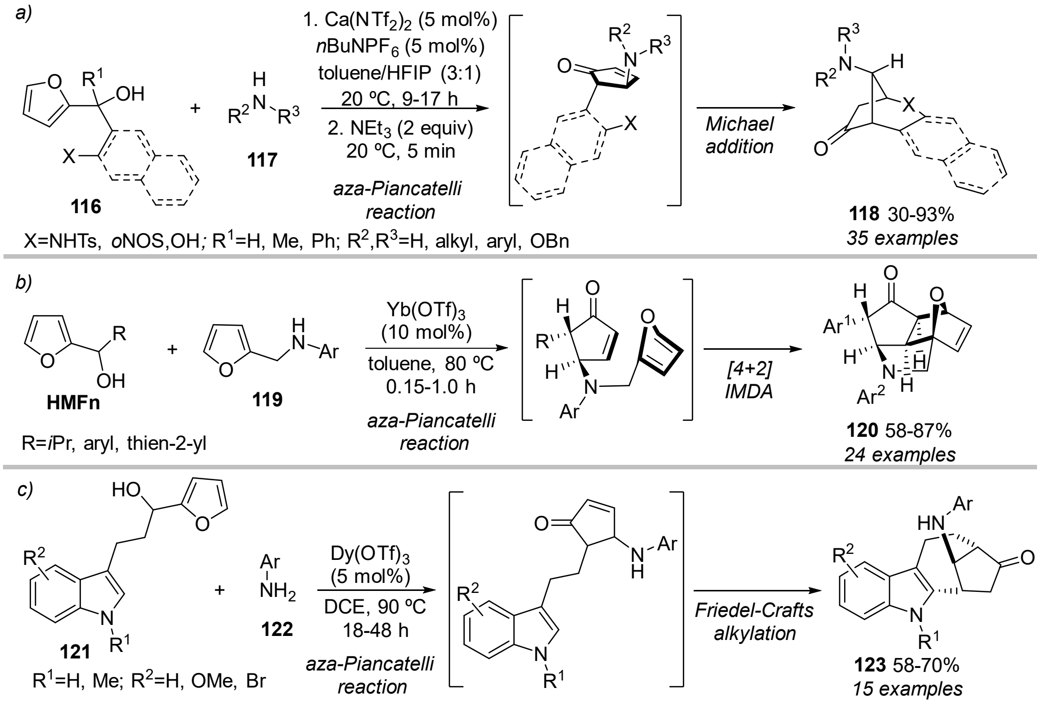
114 85-88% (X=S)
115 73-80% (X=O)
14 examples

Scheme 46. Domino aza-Piancatelli/hetero-Michael addition promoted by In(OTf)$_3$.

Since this seminal work, different research groups have explored this synthetic approach to achieve molecular complexity and diversity.[134] A two-step one-pot sequence towards bridged tetrahydrobenzo[*b*]azepines **118**, starting from furan **116** and amines **117**, based on an aza-Piancatelli cyclization/Michael addition sequence has been recently disclosed (Scheme 47a).[124] The authors envisioned that the addition of base (*e.g.* NEt_3) after completion of the $Ca(NTf_2)_2$-promoted aza-Piancatelli reaction would trigger the Michael addition leading to the desired products. The method tolerates a wide range of functional groups giving access to important scaffolds in organic synthesis. A highly efficient and diastereoselective reaction sequence for the synthesis of cyclopenta[*b*]piperazinones *via* an aza-Piancatelli cyclization/aza-oxyallyl cation trapping between 2-furylcarbinols, anilines and α-haloamides was accomplished by the same group.[123]

Baskaran and co-workers developed a general route for the construction of angularly fused 5-6-5 aza-tricyclic framework through the combination of aza-Piancatelli rearrangement and intramolecular Diels-Alder reaction (IMDA) as the key step (Scheme 47b).[118] Within the several catalysts screened for this transformation, $Yb(OTf)_3$ was found to be the most efficient to perform the reaction between HMFn and *N*-(furan-2-ylmethyl)anilines **119**, affording the hexahydro-2*a*,5-epoxy-cyclopenta[*cd*]isoindole derivatives **120** in high yield and short reaction time. Further transformations of these adducts, namely the BBr_3-promoted cleavage of the oxa bridge, allowed the formation of an aza-tricyclic bromohydrin, an aza-tricyclic BCE core of a gracilamine alkaloid, illustrated the synthetic potential of these compounds.

The development of sequential Piancatelli cyclization/Friedel-Crafts alkylation synthetic routes has given access to valuable scaffolds. Using this strategy, a diversity of cyclopenta[*f*]pyrrolo[1,2-*d*][1,4]diazepinones have been efficiently prepared employing HMFn and (1*H*-pyrrol-1-yl)anilines as reaction partners, and $In(OTf)_3$ as catalyst.[117]



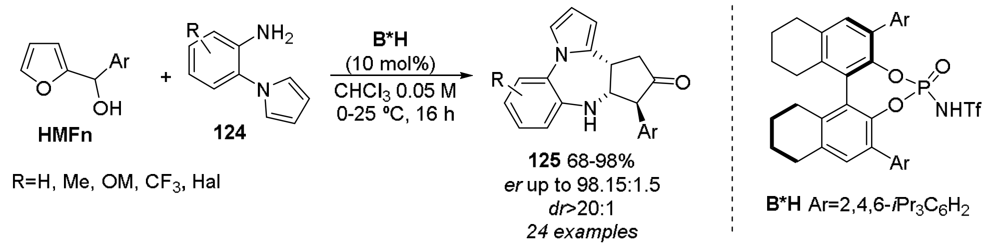
Scheme 47. Catalytic domino sequences involving the aza-Piancatelli reaction.

Additionally, indole-tethered HMFn **121** reacted with a variety of anilines **122** in the presence of 5 mol% of $Dy(OTf)_3$ to generate *in situ* the corresponding 4-arylcyclopentenones, which underwent a Friedel-Crafts alkylation at the indole's C2 position to provide selectively a range of *cis*-bridged cycloocta[*b*]indolone derivatives **123** in yields ranging from 58 to 70% (Scheme 47c).[135] The reaction outcome was influenced by the length of indole's tethered side-chain, with substrates containing shorter side-chains (*e.g.* 2 carbons) failing to undergo the second step of the domino sequence whereas substrates bearing a longer side-chain (*e.g.* 4 carbons) afforded a cyclized by-product resulting from the more favourable indole addition to the furfuryl cation.

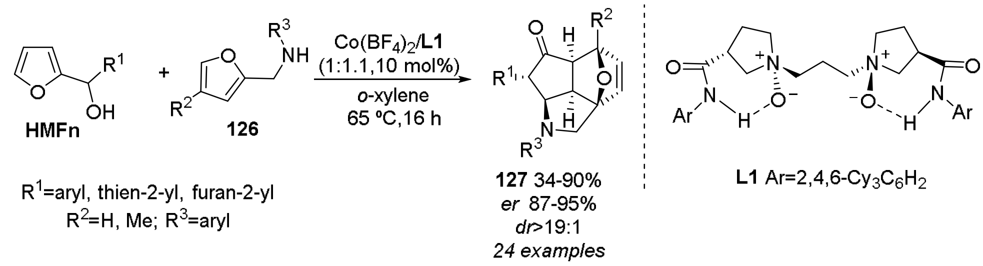
Despite the recent progresses, enantioselective versions of these domino cascade sequences are still very scarce. Following the work of Subba Reddy's group,[117] Jiang and co-workers established a general protocol to enantioenriched cyclopenta[*f*]pyrrolo[1,2-*d*][1,4]diazepinones **125**, starting from HMFn and amines **124**, using an octahydro-BINOL-derived *N*-triflylphosphoramide as chiral Brønsted acid (Scheme 48a).[136] The cascade aza-Piancatelli cyclization/Friedel-Crafts alkylation reaction proceeded with high degree of chemo-, enantio- and diastereoselectivities providing the target products **125** with three contiguous stereocenters in up to 98% *ee*. Control experiments were carried out demonstrating that the aza-Piancatelli cyclization is the stereoselective-determining step, since the intramolecular Friedel-Crafts-type conjugate addition on the isolated intermediate in the presence of an achiral catalyst led to the final product with retention of the intermediate's stereoselectivity.

Inspired by Bascaran's work,[118] Feng and co-workers envisioned that a chiral *N,N'*-dioxide/Co^{II} complex tolerant to water could induce enantiocontrol into the aza-Piancatelli rearrangement/Diels-Alder cascade reaction towards hexahydro-2*a*,5-epoxy-cyclopenta[*cd*]isoindole derivatives **127** (Scheme 48b). Indeed, a wide range of HMFn and *N*-(furan-2-ylmethyl)anilines **126** reacted smoothly in the presence of the metal salt $Co(BF_4)_2$ and *L*-proline-derived ligand **L1** (1:1.1, 10 mol%) in heated *o*-xylene to yield the desired products **127** with excellent diastereo- and enantioselectivities. Moreover, the enantioselectivity of the transformation was strongly influenced by the steric hindrance of the ligand's aniline subunits, with **L1** bearing a bulky 2,4,6-cyclohexyl aniline moiety being the most efficient.

a) Aza-Piancatelli rearrangement/Friedel-Crafts alkylation



b) Aza-Piancatelli rearrangement/Diels-Alder reaction

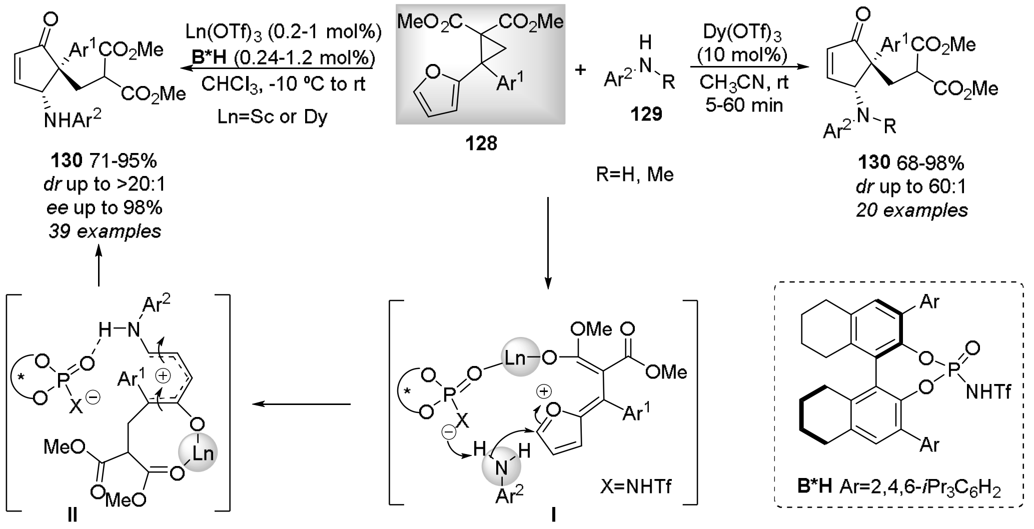


Scheme 48. Catalytic enantioselective domino sequences involving the aza-Piancatelli reaction.

The aza-Piancatelli rearrangement still has some limitations, especially when tertiary HMFn are used as substrates. In this case, a competitive dehydration pathway may occur leading to a significant decrease in the yield of the desired rearrangement product. To overcome this issue, alternative methods with other furan derivatives capable of generating the furanoxonium ion intermediate have been developed.

The Read de Alaniz's group established a new platform for triggering the rearrangement by using for the first time donor-acceptor cyclopropanes **128** (D-A CPs) as substrates (Scheme 49).[137] These highly strained rings readily react with a range of anilines **129** under Dy(OTf)$_3$-catalysis giving access to the corresponding 4-aminocyclopentenones **130** bearing α-quaternary carbon stereocenters in good to excellent yields.

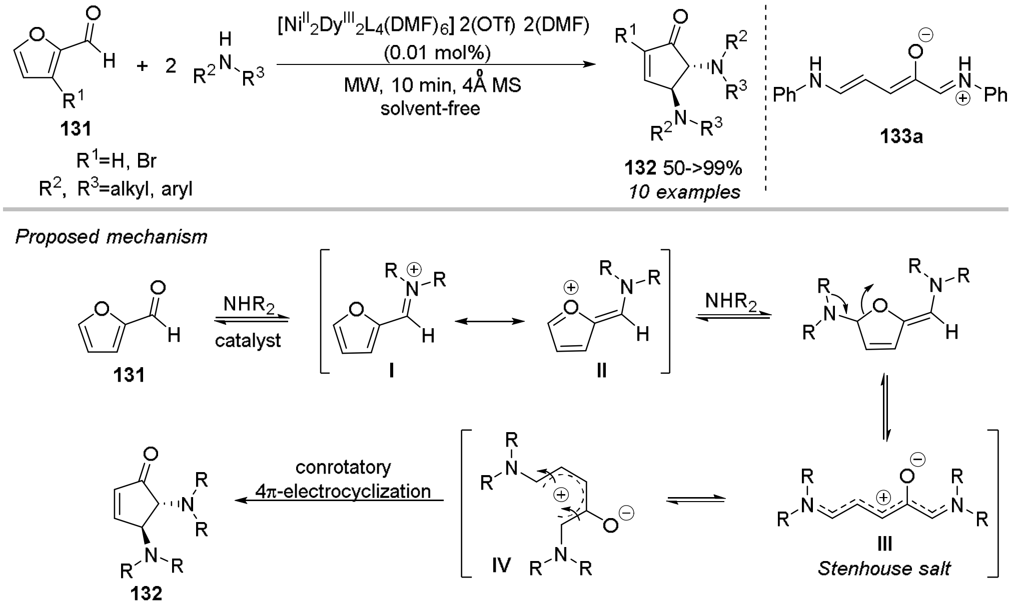
The asymmetric variant of this interesting cascade ring-opening/aza-Piancatelli rearrangement reaction has been recently achieved by Cai and Tang using Lewis acid and chiral Brønsted acid cooperative catalysis (Scheme 49).[116] The combination of strong Lewis acids such as Ln(OTf)$_3$ salt with chiral octahydro-BINOL-derived *N*-triflylphosphoramide allows the generation of (NTPA)Ln(OTf)$_2$ species (*N*-triflylphosphoramide anion, NTPA) by ligand exchange, which promotes the cyclopropane ring-opening of **128** to originate a stabilized oxocarbenium enolate-Ln^{III} intermediate **I**. Subsequent NTPA anion-mediated nucleophilic attack by the amine with concomitant Ln^{III}-assisted furan ring-opening leads to carbocation **II**, which undergoes a 4π-electrocyclization process with high enantiocontrol induced by the presence of the chiral Brønsted acid anion in one of the carbocation's faces. Under this effective dual catalyst system, a wide range of optically active functionalized cyclopentenones **130** were accessed with excellent enantio- and diastereoselectivities. It is noteworthy that a notable low catalyst loading (0.2-1.2 mol%) was employed to achieve these results.



Scheme 49. Aza-Piancatelli rearrangement of donor-acceptor cyclopropanes.

Furfural derivatives are also compatible substrates for this type of rearrangement leading to the selective formation of *trans*-3,5-diaminocyclopent-2-enones **132** by reacting with 2 equivalents of an amine (Scheme 50). Since the initial report by Lewis in 1979, several research groups have explored this transformation by employing different catalytic systems and reaction media.[138] In 2007, Batey and co-workers developed an efficient Dy(OTf)$_3$-promoted methodology for the preparation of *trans*-4,5-diaminocyclopentenones and later applied it to the total synthesis of natural product (±)-Agelastatin.[139,140] Following this pioneering work, alternative methods have emerged such as the use of ionic liquid 1-methylimidazolium tetrafluoroborate[141] as a reusable catalyst, AlCl$_3$[119] in acetonitrile, Cu(OTf)$_2$[142] in water, ErCl$_3$[143] in ethyl lactate as more eco-friendly system, and also ErCl$_3$ immobilized on silica[144] under heterogeneous conditions. Additionally, the organocatalyzed reaction of 2-furaldehyde with secondary aliphatic amines in the presence of *p*-toluenesulfonamide in heated acetonitrile, was disclosed by Wang and co-workers.[145] An alternative catalyst-free strategy for the efficient preparation of *trans*-4,5-diaminocyclopentenones in water under microwave irradiation (60 ºC, 5 min) was accomplished by Nardi and co-workers.[146]

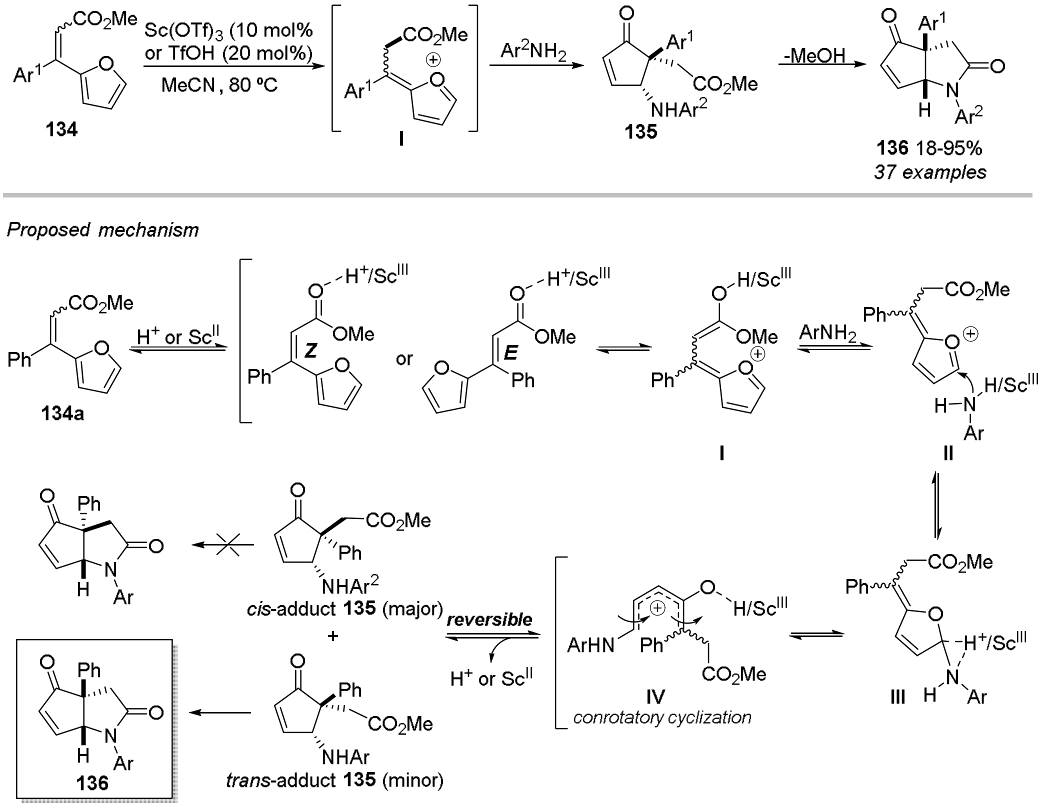
The Kostakis group developed a series of air stable bimetallic tetranuclear $Ni^{II}_2Ln^{III}2$ (Ln=Dy[147] or Y[148]) clusters which display remarkable catalytic activity in the reaction of furfurals **131** and primary or secondary amines in acetonitrile affording the *trans*-3,5-diaminocyclopent-2-enones or the corresponding Stenhouse salts[149,150] intermediates in high yields. Upon acidic conditions, the Stenhouse salts were efficiently converted into the target products by ring-closure reactions. This work has been recently extended to the synthesis of catalyst $[Ni^{II}_2Dy^{III}2L_4(DMF)_6]$ 2(OTf) 2(DMF) using (*E*)-2-(((2-hydroxyphenyl)imino)methyl)-6-methoxyphenol as ligand, which showed an enhanced catalytic efficiency when compared with the previous methods.[151] In the developed methodology, a range of primary and secondary amines reacted with furfural as well as with 3-bromofurfural in the presence of 0.01 mol% of the catalyst under solvent-free microwave-assisted conditions to provide the desired products **132** in short reaction times (Scheme 50). Moreover, theoretical and crystallographic (*e.g.* Stenhouse salt **133a**) studies demonstrated that this transformation proceeds *via* a 4π-conrotatory electrocyclization process, a key step in the domino ring-opening/electrocyclization reaction.



Scheme 50. Catalyzed aza-Piancatelli rearrangement from furfural.

In 2022, Cai and co-workers broadened the scope of the Piancatelli reaction by developing a novel methodology that employs methyl furylacrylates **134** as a new type of functionalized furanoxonium precursors (Scheme 51).[152] Under TfOH or $Sc(OTf)_3$ catalysis, these interesting intermediates reacted smoothly with a wide range of anilines in heated acetonitrile giving access to cyclopenta[*b*]pyrrolidinones **136** in moderate to excellent yield. The surprising formation of bicyclic γ-lactams **136** was rationalized as resulting from a *retro*-aza-Piancatelli rearrangement of the major *cis*-fused cyclopentenone **135** into the minor *trans*-fused isomer followed by a lactamization reaction. Control experiments and kinetic studies revealed that both (*E*)-**134** and (*Z*)-**134** give rise to the same products, although the (*Z*)-**134** isomer presented a higher reactivity. In addition, it was observed that in the presence of TfOH or $Sc(OTf)_3$ *cis*-**135** was converted into the product **136,** along with the formation of the starting reagents **134** and aniline, demonstrating the reversibility of the aza-Piancatelli reaction. The proposed mechanism involves the formation of furanoxonium ion intermediate **I** through the acid activation of the carbonyl group of methyl furylacrylate **134**, followed by the acid-mediated nucleophilic addition of the aniline to give intermediate **III**. Subsequent furan ring-opening/isomerization originates the pentadienyl carbocation **IV**, which undergoes a 4π-electrocyclization to afford a mixture of *cis*- and *trans*-**135**. The latter can undergo lactamization to cyclopenta[*b*]pyrrolidinones **136** whereas the former is converted into the *trans*-**135** *via* a *retro*-aza-Piancatelli rearrangement.

An innovative three-component synthetic approach based on the radical-mediated Piancatelli-type rearrangement of furyl-substituted terminal alkenes with a wide variety of fluoroalkyl radical precursors and anilines has been accomplished by the same group.[153] The catalytic protocol involves the combination of copper (I) or photoredox catalysis with chiral Brønsted acid and unchiral Lewis acid catalysis featuring a wide substrate scope. The 5-alkyl-5-aryl-4-(arylamino)cyclopentenone derivatives were obtained with high diastereo- and enantioselectivity (up to 96% *ee*).

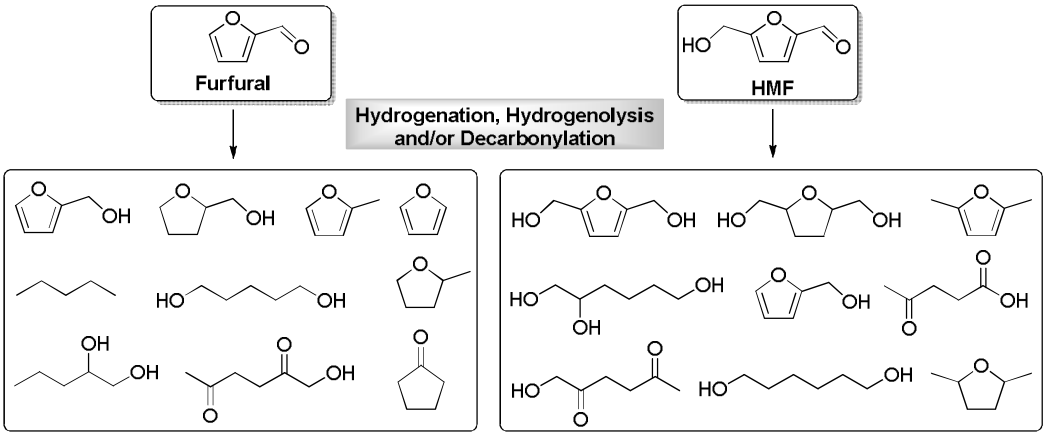


Scheme 51. Cascade rearrangement/lactamization of methyl furylacrylates.

4. Metal-catalyzed furan ring-opening reactions

The presence of highly reactive multiple sites/functionalities in furfural (FF) and hydroxymethylfurfural (HMF), such as the aldehyde group, the hydroxy group, and the aromatic furan ring, enables them to successfully participate in several catalytic transformations.[154,155] Within these processes, hydrogenation and hydrogenolysis of FF and HMF provides access to a range of molecules such as furfuryl alcohol (HMFn), 2,5-bis(hydroxymethyl)furan (BHMF), 2,5-bis(hydroxymethyl)tetrahydrofuran (BHMTHF), methylfurfural (MF), 2,5-dimethylfuran (DMF), 1-hydroxyhexane-2,5-dione (HHD), tetrahydrofuran (THF), among others, whose preferential formation depends on the nature of catalysts, the reaction temperature, and pressure

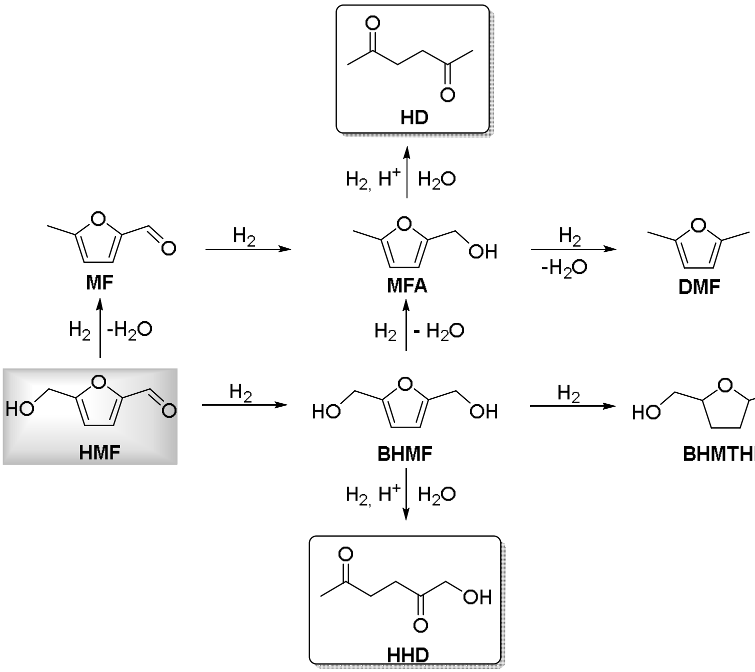
(Scheme 52). Different catalytic methodologies involving monometallic and bimetallic heterogeneous and homogeneous catalysts have been extensively studied in order to achieve selectivity in these highly challenging transformations. Among the heterogeneous catalysts, the most frequently used are based on supported metals such as Pd, Pt, Ni, Ru on C, and Pd on SiO_2, TiO_2 or Al_2O_3, whereas homogenous catalysts include Rh, Ru or Ir complexes with bidentate *N*-heterocyclic carbenes, primary amine moieties, and gold sub-nanoclusters. These topics have been extensively reviewed by different authors in recent years. For example, Zhang and co-workers reviewed the catalytic transformation of biomass-derived compounds into valuable chemicals and fuels in the presence of magnetic catalysts, whereas Singh and co-workers described various catalytic processes for the production of value-added compounds from furfural and HMF under heterogeneous metal catalysis.[156,157] More recently, the catalytic hydroconversion of HMF to biomass-derived diols (*e.g.* BHMF, BHMTHF, DMTHF and 1,6-hexanediol) was reviewed by Liu and Yang,[158] and Sels and Makshina.[159] The recent advances in heterogeneous catalytic transfer hydrogenation/hydrogenolysis (CTH) of furfural and HMF were also recently reviewed by Jin and Riisager.[160,161] In this section, some selected examples on the catalytic hydrogenation/hydrogenolysis of HMF will be highlighted.



Scheme 52. Transformation of furanic platform chemicals furfural and 5-hydroxymethylfurfural into various value-added chemicals.

The major products arising from both hydrogenation and hydrogenolysis processes of HMF are illustrated in Scheme 53, with these transformations occurring competitively if an acidic medium is provided. Several efficient protocols for the selective formation of these products have been accomplished. For example, the use of supercritical carbon dioxide-water over 5 wt% Pd/C under a combined atmosphere of CO_2 (100 bar) and H_2 (10 bar) at 80 ºC, led to DMF in 100% yield within 2 hours.[162] A bimetallic catalyst comprised of a Lewis-acidic Zn(II) and Pd/C at 150 ºC under 22 bar of H_2 also effectively promoted the formation of DMF in 85% yield.[163] Additionally, a complete conversion of HMF into DMF was attained employing a Ru/C catalyst at 200 ºC and 20 bar of H_2 in THF solution.[164] In a different protocol, the selective hydrogenation of HMF to furan diols was achieved by using a Ru/C catalyst with low metal loading (1 wt%).[165] The fine tuning of the reaction conditions allowed the isolation of BHMF in 93% yield (50 ºC and 30 bar H_2) and BHMTHF in 95% (100 ºC and 50 bar H_2). On the other hand, by using carbon-supported Pd nanoparticles as the catalysts and formic acid as the hydrogen source at 200 ºC under 5 bar of N_2, methylfuran (MF) was formed selectively in 80% yield.[166]

Another product resulting from the hydrogenolysis of HMF is HHD (Scheme 53). Reaction conditions and results of some selected protocols for this transformation are depicted in Table 1 and include various homogeneous and heterogeneous catalysts.[167-175] It is worth noting that most of the reported yields and selectivity were determined by GC analyses. An exception was the work developed by de Vries and co-workers that reported the isolated yield of HHD (69%) obtained by promoting the reaction of aqueous HMF in the presence of the half-sandwich [Cp*Ir(dpa)Cl)Cl] complex at 120 ºC and 10 bar of H_2.[173]



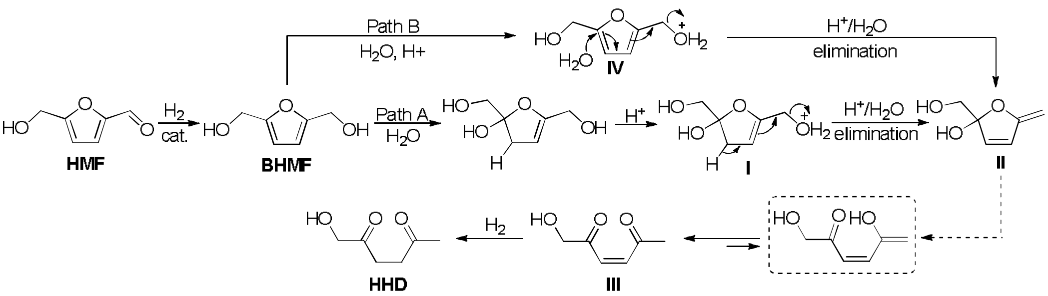
Scheme 53. Major hydrogenation and hydrogenolysis products from 5-hydroxymethylfurfural.

Table 1. Selected protocols for the conversion of HMF into HDF.

Entry	Catalyst	T (ºC)	P (bar)	HHD Yield (%)[a]	Sel. (%)	Ref.
1	Pd/Nb_2O_5	140	40	93	73	167
2	Ir-complex	120	5	84	84	168
3	Pd/MIL-101(Cr)	140	40	82	83	169
4	Pd/C, AcOH	120	40	68	71	170,171
5	$Rh-Re/SiO_2$	120	80	81	81	172
6	Ir-complex	120	10	76 (69)[b]	76	173
7	Pd/Beta Zeolite	110	40	61	61	174
8	Ru/C, IL	100	50	100	99	174,175

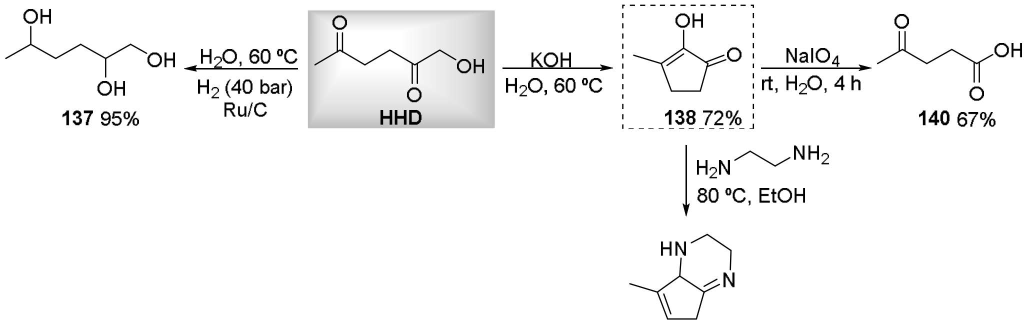
[a]Yield and selectivity determined by GC analyses. [b]Isolated yield.

Recently, the first example of the hydrogenation/hydrogenolysis of HMF with Ru/C as the catalyst under batch multiphase and continuous-flow conditions, was disclosed by Selva and Luque.[175] Notably, by simply changing the reaction parameters, high selectivity was achieved for the formation of three different products: BHMF (92%), BHMTHF (90%), and HHD (99%). A mechanistic pathway for the hydrolytic ring-opening of HMF to HHD was proposed involving the hydrogenation of HMF into BHMF as the first step (Scheme 54). The latter can undergo two different pathways that lead to the same intermediate **II**. In pathway A, a regioselective 2,3-addition of H_2O followed by a OH-protonation occurs originating intermediate **I**, which undergoes a concerted elimination to give intermediate **II**. Alternatively, this intermediate can be formed by OH-protonation of BHMF to afford **IV** and subsequent one-step hydrolysis (pathway B). Intermediate **II** is converted into an enol through a ring-opening reaction followed to tautomerization to the α,β-unsaturated carbonyl compound **III**. The final step involves the hydrogenation of **III** to afford the desired HHD.[176]



Scheme 54. Proposed mechanism for the conversion of HMF into HHD.

In some cases, the aforementioned processes involve a multistep protocol in which HHD is formed in the initial step and is used in the construction of other products such as 1,2,5-hexanetriol **137**[171] and 2-hydroxy-3-methylcyclopent-2-enone **138** (MCP)[167,173], obtained by a catalyzed intramolecular aldol condensation (Scheme 55). Further transformations of MCP **138** lead to various cyclopentenone-derived compounds (*e.g.* **139**) and to levulinic acid **140**,[173] a versatile precursor of an array of compounds with a variety of applications.[177]



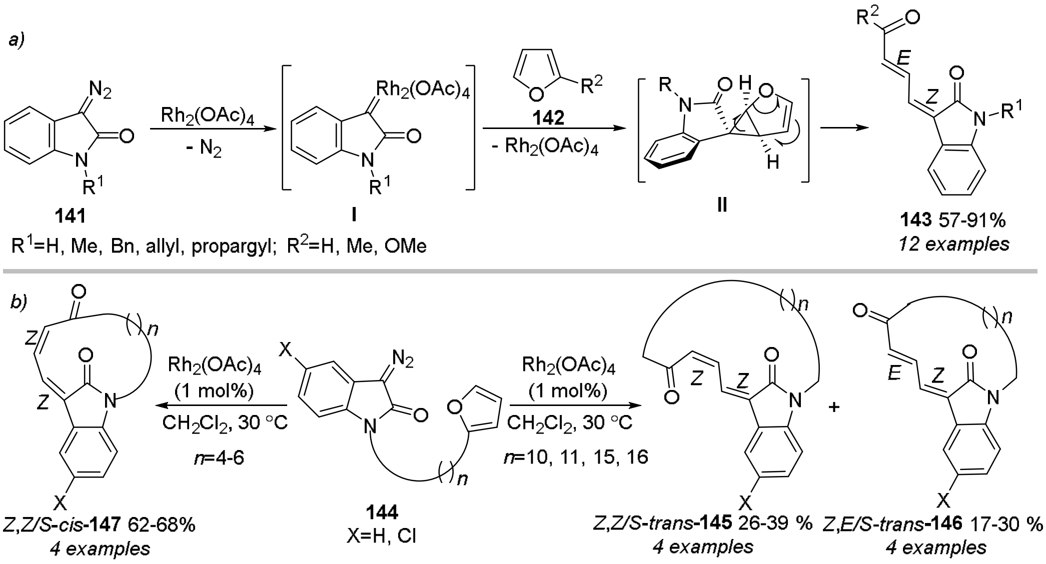
Scheme 55. Examples of HHD conversion into value-added compounds.

The production of 2,5-hexanedione (HD) from HMF has also been reported. In this context, Huo and co-workers developed an eco-friendly method for the production of HD and 3-methyl-2-cyclopenten-1-one (3-MCO) through the *in situ* generation of hydrogen by water splitting with Zn, albeit high temperatures were required (250 °C).[178] Under the optimized parameters, HD and 3-MCO were obtained in 27.3% and 30.5% yield, respectively. More recently, various iodine-modified Pd supported catalysts (PdI/AlO_3 and PdI/SiO_2) efficiently promoted the formation of HD in 50.2% yield *via* sequential hydrogenation, hydrogenolysis, and ring-opening steps.[179]

Owing to their high reactivity, metallocarbenes have been extensively used in synthetic organic chemistry in various transformations. Their classical precursors, the diazo compounds, react with several transition metal catalysts such as Rh, Pd, Cu, Ru, Ir, and Fe, etc, to generate the transient electrophilic metal-carbenoids species in the reaction medium which undergo an array of reactions to form a great variety of C-C and C-X bonds.[180] Among the available catalysts, rhodium catalysts have demonstrated to be the most efficient ones for these transformations and have been successfully employed by both industry and academia.[181]

In this context, Muthusarny and co-workers explored the reactivity of isatin-derived diazoamides **141** with symmetrical and unsymmetrical furan derivatives in the presence of rhodium (II) acetate to yield a variety of (3*Z*)-3-[(2*E*)-4-oxopent-2-en-1-ylidene]indol-2-ones **143** in a regio- and diastereoselective fashion (Scheme 56a).[182] Interestingly, the stereoselectivity was controlled by the slow addition of diazoamides **141**. According to their proposed reaction mechanism, the initially formed transient rhodium(II) carbenoid **I** leads to cyclopropanation on reacting with the furan **142** originating intermediate **II**. Subsequent stereoselective ring-opening provides the desired products **143** with high diastereoselectivity.

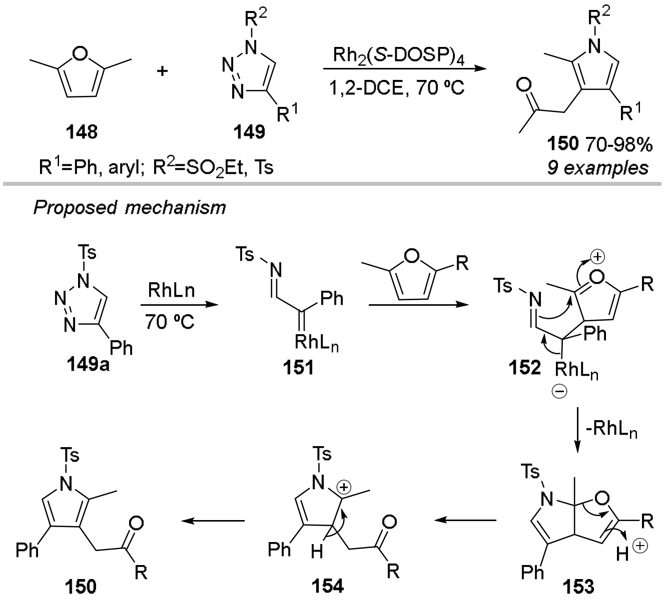
Later on, the authors developed the intramolecular variant of this methodology by employing a variety of furan tethered on diazoamides **144** as substrates (Scheme 56b).[183] This strategy gave access to 12- to 23-membered oxindole incorporated macrocyles **145**, **146** and **147** in moderate to good yields under mild reaction conditions. The stereoselective outcome was influenced not only by the concentration of diazoamides but also by the spacer length in **144**, with longer spacers affording mixtures of *Z*,*Z*/S-*trans*-**145** and *Z*,*E*/S-*trans*-**146** isomers whereas shorter spacers gave *Z*,*Z*/S-*cis*-**147** as single isomers.



Scheme 56. Rhodium-catalyzed cyclopropanation followed by furan ring-opening reactions.

The reactivity of *N*-sulfonyl-1,2,3-triazole-derived rhodium-stabilized donor/acceptor carbenes towards furan derivatives has also been explored.[184-186] Davies and co-workers developed an innovative methodology for the preparation of functionalized pyrroles **150** based on the reaction of rhodium-stabilized imino-carbenes **151**, generated *in situ* from *N*-sulfonyl-1,2,3-triazoles **149**, with symmetrical and unsymmetrical 2,5-dialkylfurans (*e.g.* **148**) under mild reaction conditions (Scheme 57).[184] The reaction proceeds through initial [3+2]-annulation of **152** to give bicyclic hemiaminals **153**, followed by acid-catalyzed ring-opening to give **154** which undergoes aromatization to provide the target pyrroles **150** in high yields.

A different outcome was observed by Murakami and Miura in the rhodium(II)-catalyzed reaction of *N*-sulfonyl-1,2,3-triazoles with 2-(siloxy)furans **155** (Scheme 58).[185] In this case, the stereoselectivity of the cyclopropanation process was strongly influenced by the ligand with cyclic 1,2-dihydropyridines **156** or open-chain penta-2,4-dien-1-imines **157** being selectively formed in good to excellent yields. The use of catalyst $Rh_2(esp)_2$ (esp=α,α,α',α'-tetramethyl-1,3-benzenedipropionate) favored the formation of **156** whereas sterically bulkier *N*-naphthoyl-*tert*-leucinate (NTTL) ligand led to penta-2,4-dien-1-imines **157** as single products. This was rationalized as resulting from the preferential formation of the diastereoisomeric transition states **I** (path A) or **III** (pathway B) starting from intermediate **158**, followed by ring-opening in a stereospecific fashion to afford compound **157** and intermediate **V**, respectively (Scheme 58). The latter, with the C2 double bond in *Z* configuration, undergoes spontaneous 6π-electrocyclization to the target 1,2-dihydropyridines **156**. In addition, a two-step one-pot procedure towards penta-2,4-dien-1-imines was also successfully accomplished starting from mesyl azide and phenylacetylene, with the *in situ* generation of the corresponding *N*-mesyl-1,2,3-triazole.

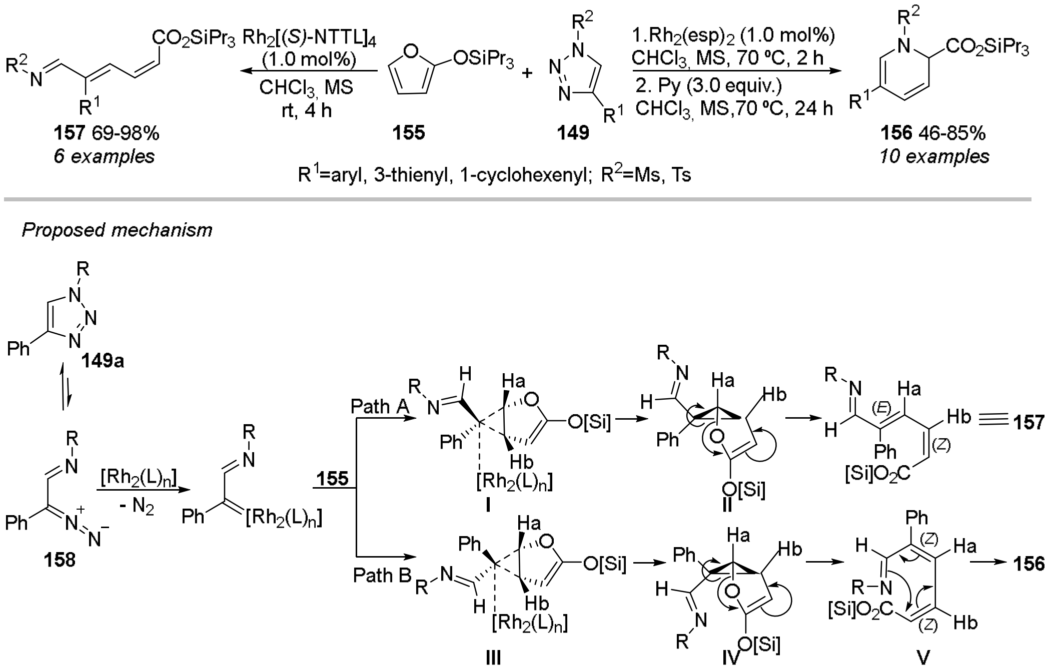


Scheme 57. Rhodium-catalyzed conversion of furans into pyrroles.

More recently, Uchuskin and Hashmi developed a straightforward protocol for the synthesis of 2-formyl- and 2-acetylpyridine derivatives by exploring the one-pot intramolecular rhodium-promoted reaction of 1-tosyl-1,2,3-triazoles with furans (Scheme 59).[186] Starting from readily accessible (furyl-2-ylmethyl)propargyl amines (X=NR^4) or ethers (X=O) **159**, a series of 2-formyl- and 2-acetylpyridines **160** and **161**, respectively, were obtained in moderate to excellent yields. This cascade process involves initial copper-catalyzed azide-alkyne cycloaddition (CuAAC) to generate intermediate **162**, which undergoes $Rh_2(OOc)_4$-mediated denitrogenative decomposition to spiro-intermediate **I** followed by ring-opening rearrangement to give azatriene **II**. The final product arises from 6π-aza-electrocyclization of dihydropyrrole **II** to the corresponding bicycle **163**, followed by Et_3N-promoted aromatization through elimination of sulfinate (Scheme 59). Additionally, an alternative reaction pathway was observed when substrates bearing extended linkers between the triazole moiety and the furan ring were studied, providing different heterocyclic systems such as fused pyrroles.

The furan ring has also been explored as a privileged substrate for both intra- and intermolecular gold-promoted transformations. Its high nucleophilicity makes them the ideal reaction partner with π-systems activated by the coordination of gold. Prandi and Nejrotti have recently reviewed the synthesis and functionalization of furans *via* gold catalysis, including the reactions involving furan ring-opening. Selected examples of these transformations will be highlighted.[187]

A site-selective and divergent Au^{III}-catalyzed synthetic approach to 2-aminopyrroles and quinolone-fused polyazaheterocycles has been accomplished by Hashimi and co-workers (Scheme 60).[188] This one-pot strategy explored the chemical behavior of anthranils **164** and *N*-furanylmethylynamides **165** under $KAuBr_4$ catalysis uncovering a novel reactivity. Surprisingly, instead of the expected tetracyclic *N*-heterocycles derived from the C3-H insertion into the gold carbene, pyrroles (*E*)-**166** were formed. In addition, the formation of the thermodynamically less stable derivatives (*Z*)-**166** could also be achieved when the synthetic procedure did not include the final heating step. The key step for this successful tandem reaction is the regioselective attack of the C2 position of the furan moiety to the *in situ* generated α-imino gold carbene species **A1** to generate spiro-intermediate **B2** (pathway B). Subsequent furan ring-opening followed by aromatization originates (*Z*)-**166**, which can be further transformed into the thermodynamically stable pyrroles (*E*)-**166** or to tricyclic azaheterocycles (*E*)-**167** through a Friedel-Crafts-type cyclization promoted by heating and/or a Lewis acid.



Scheme 58. Rhodium-catalyzed reaction of *N*-sulfonyl-1,2,3-triazoles with 2-(siloxy)furans.

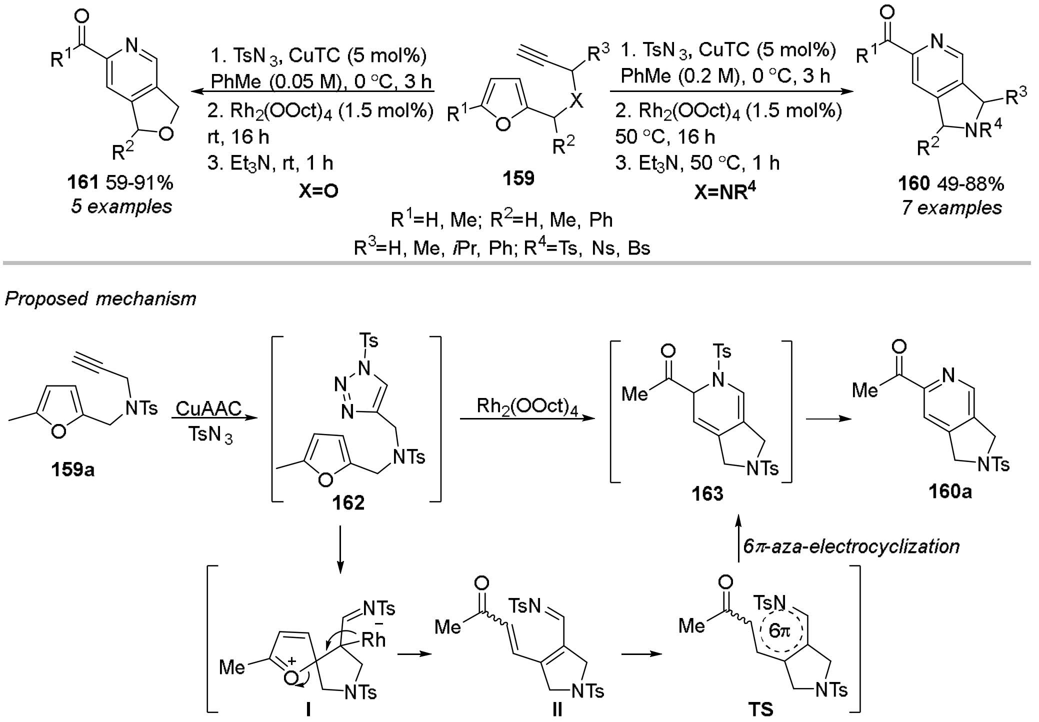
Another methodology involving furan ring-opening describes the gold-catalyzed cascade transformation of Ugi adducts **168** into 2-pyridinones **169** (Scheme 61).[189] After the initial furan-alkyne cyclization to yield intermediate **I**, this undergoes furan ring-opening and cleavage of the isocyanide-originated fragment to afford selectively *cis*-2-pyridinones **169**. Most interestingly, these derivatives upon prolonged exposure to a strong Brønsted acid spontaneously isomerize into the more stable *trans*-2-pyridinones **169**, thus providing access to both isomers.

The reactivity of *N*-furanylmethylynamides towards quinoline *N*-oxides in the presence of a Au(I) catalyst has also been explored opening the way to the selective formation of functionalized dihydropyridinones and pyranones.[190]

Another type of unsaturated π-systems that are susceptible to activation by cationic Au^I catalysts are allenes. An efficient protocol for the preparation 2-spiroindolin-3-ones based on Au(IPr)NTf_2-mediated ring-opening/ring-closing cascade reactions of furoindoles and allenamides has been recently disclosed (Scheme 62).[191] The cascade sequence proceeds through the addition of the gold-activated allene **171** to the furan moiety of furoindoles **170** to give intermediate **I**, followed by a ring-opening/ring-closing process to originate 2-spiroindolin-3-ones **172** in moderate to good yields.

5. Acid-catalyzed furan ring-opening reactions

The Butin reaction is the acid-catalyzed transformation of furans, having a nucleophilic group tethered to the α-carbon atom, into various functionalized heterocycles. The intramolecular attack of the nucleophile to the furyl α-carbon atom gives a spirocyclic intermediate, which rearranges to the final product by a furan ring-opening reaction (Figure 4).[192,193] This acid-catalyzed transformation has been used in the synthesis of various heterocycles, such as benzofurans, indoles, isocoumarin and isoquinoline derivatives, pyrrolodiazepines, pyrrolopyrazines, among others, summarized in a review published in 2016.[193]

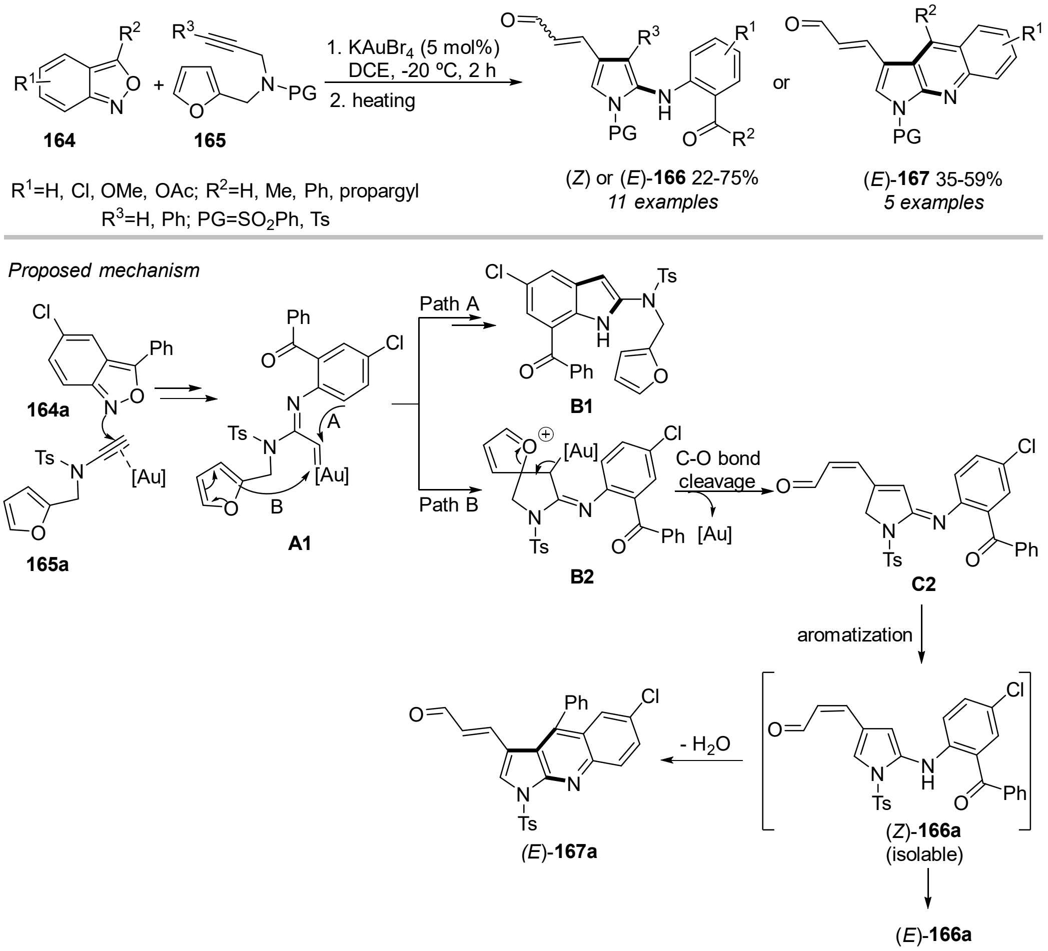


Scheme 59. Intramolecular rhodium-catalyzed reaction of 1-tosyl-1,2,3-triazoles with furans.

The first study dates back to the earlier 90's when Butin and co-workers explored the synthesis and recyclization reactions of difurylmethanes. The authors found out that the reaction of salicylaldehydes **173** and methylfuran (MF) in the presence of catalytic perchloric acid gave a mixture of difurylmethanes **174** and benzofurans **175** (Scheme 63).[194] They also observed that compounds **174** were converted into benzofurans **175**, upon treatment with $HClO_4$. Thus, the proposed mechanism for the transformations of **174** into **175** starts with the protonation of furan C2, followed by intramolecular *O*-nucleophilic attack at the α-position of the furanium ion, giving the spirocyclic intermediates **II**. The subsequent furan ring-opening and isomerization to the more stable tautomeric form leads to benzofurans **175** (Scheme 63).[195]

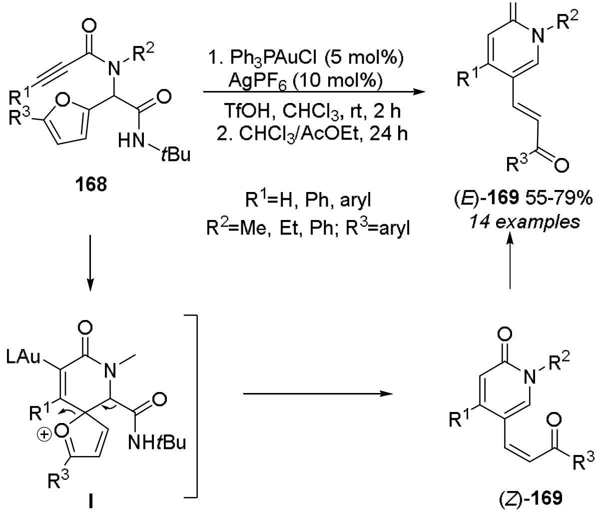
Highly substituted benzofurans were prepared by domino reactions of 2-hydroxybenzyl alcohols with furans using triflic acid (TfOH) as catalyst (Scheme 64). The acid-catalyzed reaction of 2-hydroxybenzyl alcohols **176** with 2-substituted furans gave intermediates **177**, which underwent *in situ* Butin reaction affording the final products **178** in high yields, in a one-pot procedure. This strategy was applied in the total synthesis of the natural product Sugikurojinol B.[196]

The synthesis of indole derivatives is a topic with relevance in chemistry due to its occurrence in nature and the wide range of biological and pharmacological activities.[197] Thus, Butin and co-workers explored the furan ring-opening/indole-ring closure of 2-aminobenzylfuran derivatives. Initially, they explored the reaction in a two-step approach, in which 2-aminobenzylfurans **180** were synthesized by the alkylation of furans with 2-aminobenzyl alcohols **179** and then converted into indoles **181**, by treatment with HCl/MeOH or AcOH/HCl systems (Scheme 65).[198,199] Some years later, this strategy was improved using catalytic amounts of triflic acid (TfOH) to promote both alkylation and Butin reaction, *via* the *in situ* formation of 2-aminobenzylfurans **180**. The developed methodology gave access to a wide range of indole derivatives in a one-pot procedure and in a multigram scale (Scheme 65).[200]

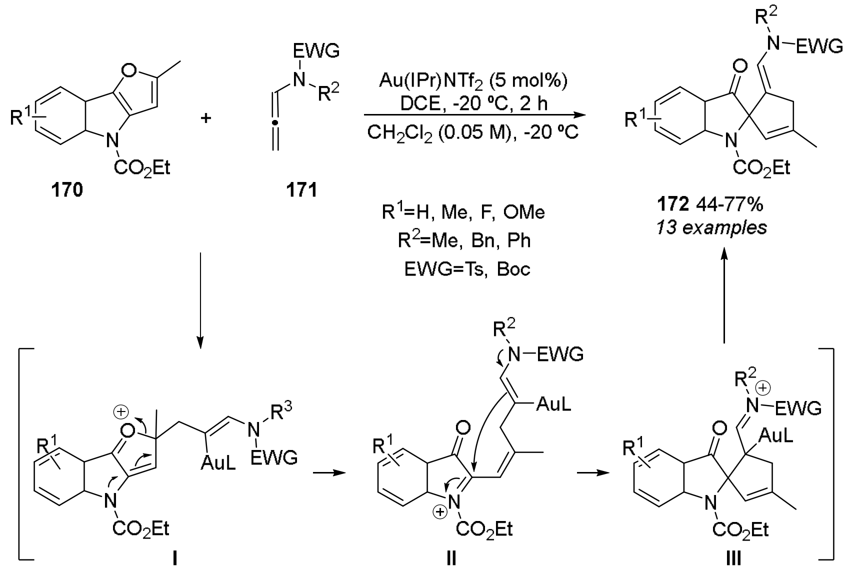


Scheme 60. Gold(III)-catalyzed synthesis of 2-aminopyrroles and quinolone-fused heterocycles.

A similar mechanism to Butin reaction, had been previously mentioned by Gilchrist and co-worker during their studies on the thermal and acid-catalyzed rearrangements of dihydro-1,2-oxazine **182a** and dihydro-1,2-pyrazine **182b**.[201] Dihydro-1,2-oxazine **182a** was converted into the open chain oxime **183** (X=O) upon treatment with trifluoroacetic acid (TFA), which was then transformed *via* spirocyclic intermediate **184** (X=O), into isoxazole **185a**. The treatment of the isolated oxime **183** (X=O) with TFA also gave the isoxazole **185a**. The same behavior was described for the transformation of dihydro-1,2-pyrazine **182b** into pyrazole **185b** (Scheme 66). Thus, Gilchrist and co-worker were the ones who reported for the first time the furan ring-opening/heterocycle ring-closing leading to heterocycles. Nevertheless, it was Butin's research group who explored this transformation for the synthesis of various heterocyclic systems.



Scheme 61. Cyclization/fragmentation sequence towards pyridin-2-ones.



Scheme 62. Synthesis of 2-spiroindolin-3-ones *via* cascade reactions of furoindoles and allenamides.

Some years later, Pinho e Melo and co-workers extended the ring-opening reactions of furans containing an oxime moiety, during their studies on the reactivity of nitrosoalkenes and azoalkenes.[202,203] The treatment of furo-oximes **186**, without substituents at position 5, with trifluoroacetic acid (TFA) afforded isoxazoles **187** in good yields (Scheme 67). On the other hand, the same reaction conditions applied to oximes **188**, gave functionalized isoxazoles **189-191** in high overall yields.[203]

Serdyuk and co-workers reported the synthesis of various pyrazolylvinyl ketones from furfuryl ketones (Scheme 68).[204] The reaction of furfuryl ketones **192** with hydrazine hydrochlorides afforded pyrazolylvinyl ketones **195**, in a one-pot procedure, through the formation of hydrazones **193** and spirocyclic intermediates **194**. In this case, additional acid-catalyst was not needed to promote the nucleophilic attack of nitrogen to C2 of the furan moiety.

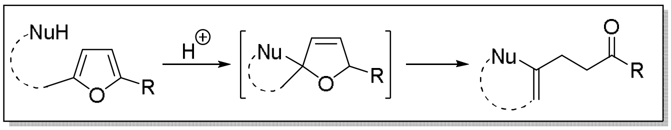
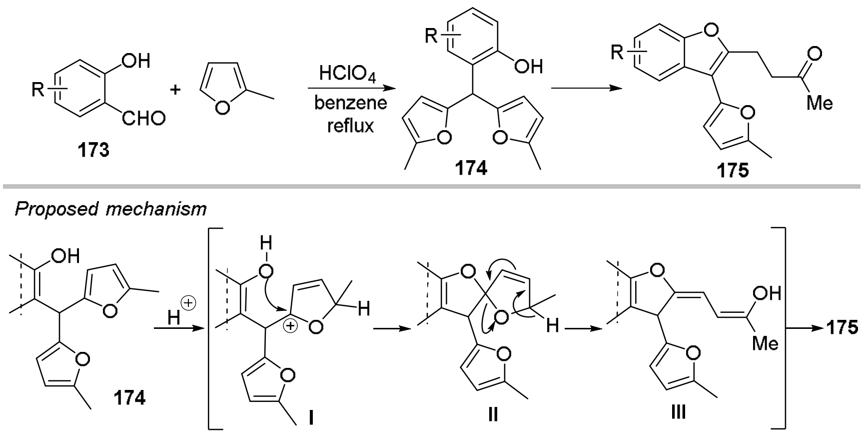
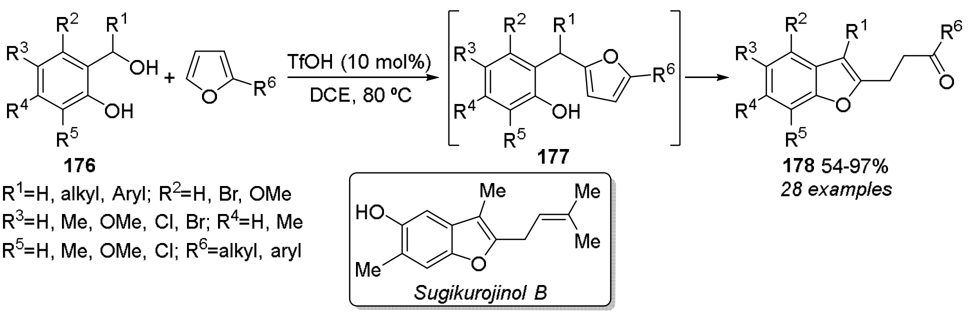


Figure 4. The Butin reaction.

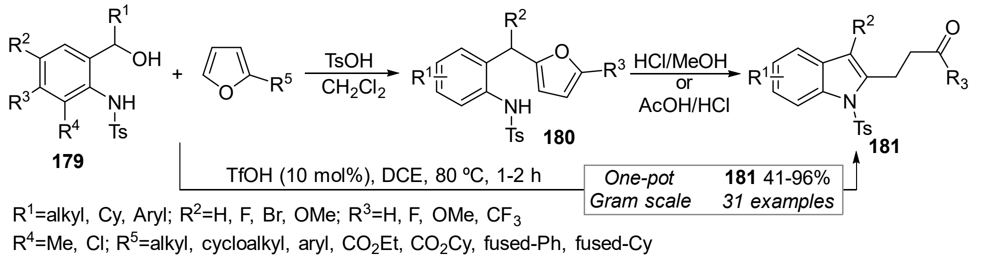


Scheme 63. Reaction mechanism proposed by Butin and co-workers for the synthesis of benzofurans from salicylaldehydes derived bisfurans.

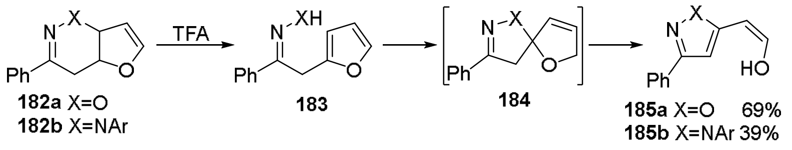


Scheme 64. Synthesis of highly substituted benzofurans through Butin reaction.

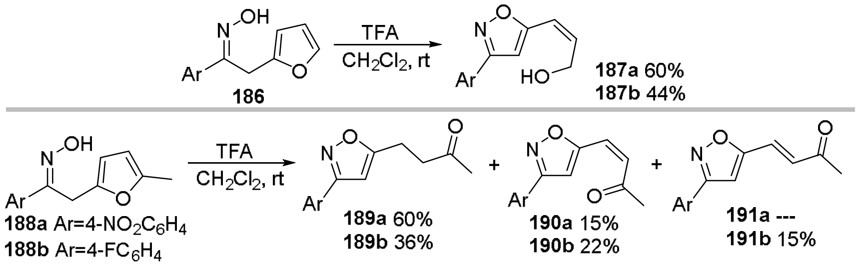
In 2016, Uchuskin and co-workers described an oxidative rearrangement of 2-aminobenzylfurans **196** to give 2-acylvinylindoles **198** in a stereoselective manner (Scheme 69).[205,206] Intermediate epoxides **I** were formed by oxidation with *m*CPBA followed by intramolecular nucleophilic attack of the amine moiety to give spirocyclic compounds **197**. The treatment of **197** with TFA promotes the dihydrofuran ring-opening and indole moiety aromatization affording (*Z*)- or (*E*)-2-acylvinylindoles **198** in high yields, in a one-pot procedure. The *Z* isomer was obtained when the phenyl group had electron-neutral or electron-deficient substituents, while electron-rich substituents led to the formation of the *E* isomer. The formation of the epoxide intermediate **I** was demonstrated by its isolation by carrying out the oxidation at lower temperature. Moreover, the spirocyclic intermediate was confirmed by the isolation of compound **197** (R^1=H, R^2=Ph, R^3=Ts, R^4=Me) in 87% yield by the addition of aqueous $NaHCO_3$ to the reaction mixture. In addition, treatment of the isolated **197** gave the corresponding 2-acylvinylindole **198** in quantitative yield. These observations supported the proposed mechanism. The *m*CPBA-promoted oxidative rearrangement was applied in the preparation of several functionalized indoles including the total synthesis of Flinderole C analogue.[205]



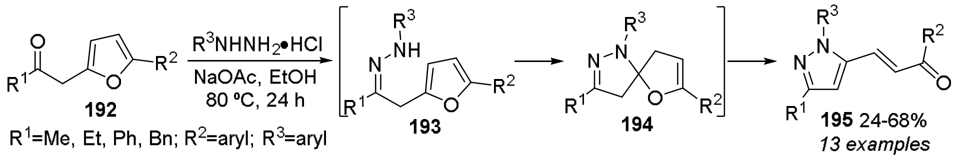
Scheme 65. Synthesis of indole derivatives through Butin reaction.



Scheme 66. Synthesis of isoxazoles and pyrazoles from dihydro-1,2-oxazine and dihydro-1,2-pyrazine described by Gilchrist and co-workers.

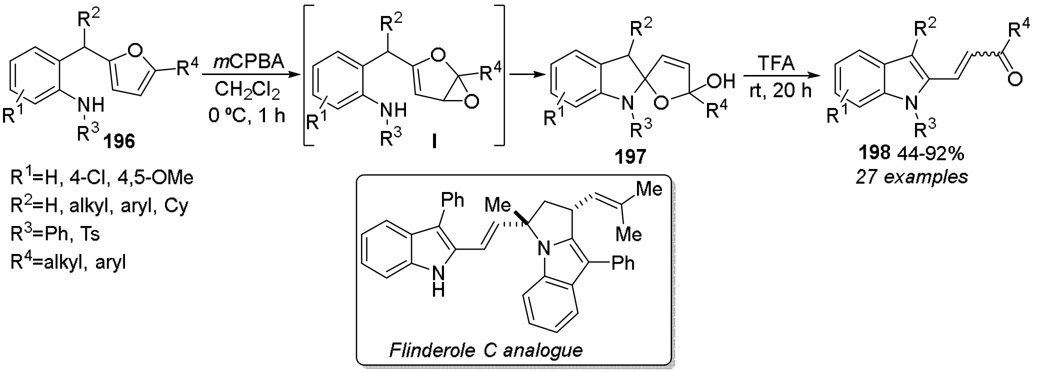


Scheme 67. Synthesis of isoxazoles from furo-oximes.

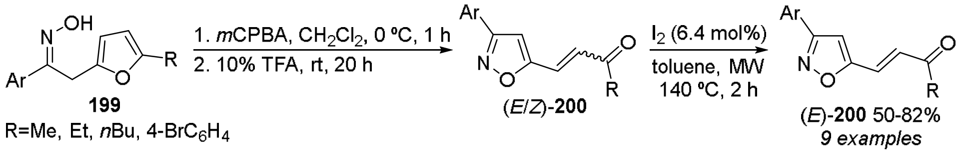


Scheme 68. Synthesis of pyrazolylvinyl ketones from furfuryl ketones.

The same reaction conditions were applied in the synthesis of isoxazolyl ketones **200** from furo-oximes **199** (Scheme 70).[207] Using this procedure *E*/*Z*-mixtures of isoxazoles **200** were obtained. However, heating this mixture in presence of catalytic iodine gave exclusively the (*E*)-isomer in good yields.

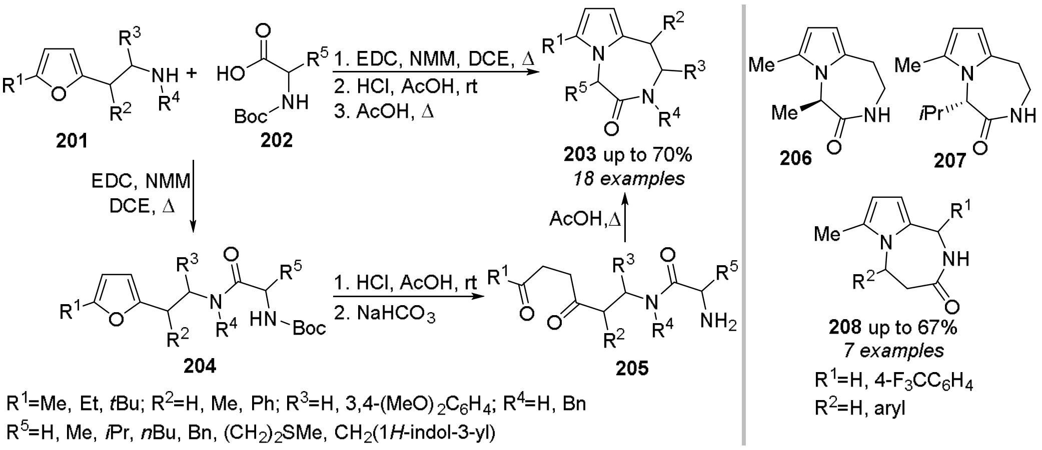


Scheme 69. Furan-oxidative rearrangement of 2-aminobenzylfurans.



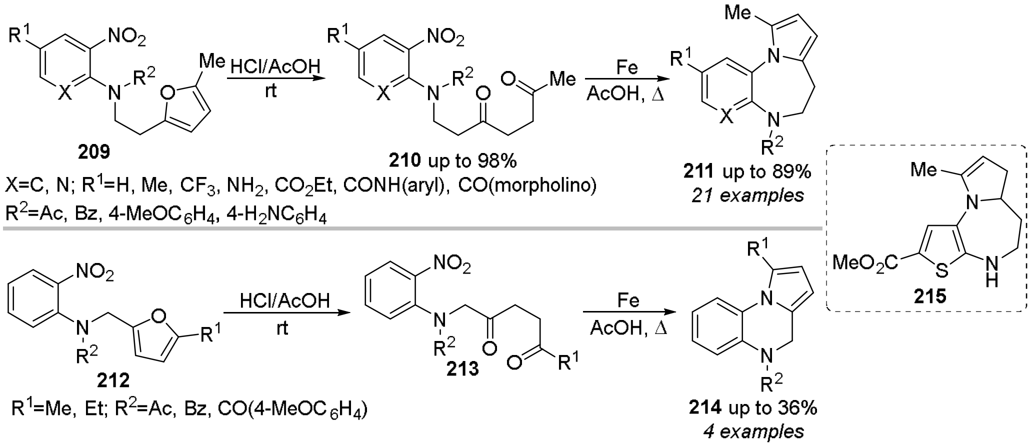
Scheme 70. Synthesis of isoxazolyl ketones from oxime-furans.

Uchuskin and co-workers explored the conversion of furans into 1,4-dicarbonyl compounds in the synthesis of polyfunctionalized pyrrolo[1,2-*d*][1,4]diazepinones (Scheme 71).[208] Thus, the reaction of 2-(furan-2-yl)ethylamines **201** with a series of *N*-Boc protected α-amino acids **202** gave, in a one-pot procedure, pyrrolo[1,2-*d*][1,4]diazepinones **203** in good yields (Scheme 71). Acylation of 2-(furan-2-yl)ethylamines **201** gave the corresponding amides **204**. Under acid conditions (HCl/AcOH), amides **204** undergo Boc cleavage and furan ring-opening affording amino-substituted 1,4-diketones **205**. Neutralization of the reaction medium and subsequent heating in acetic acid gave the pyrrole derivatives **203** through Paal-Knorr cyclization. These reaction conditions were also applied in the synthesis of chiral pyrrolo[1,2-*d*][1,4]diazepinones (**206** and **207**) using optically pure amino acids and racemic polyfunctionalized pyrrolo[1,2-*a*][1,4]diazepinones **208**.



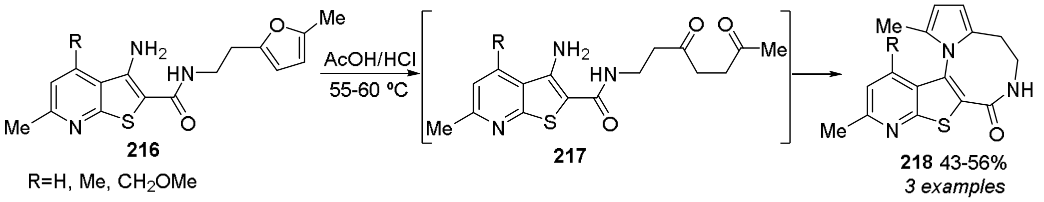
Scheme 71. Synthesis of pyrrolo[1,2-*d*][1,4]diazepinones and pyrrolo[1,2-*a*][1,4]diazepinones.

The same research group used a similar strategy to prepare functionalized pyrrolo[1,2-*d*][1,4]diazepines **211** (X=C), pyrido[2,3-*b*]pyrrolo[1,2-*d*][1,4]diazepines **211** (X=N) and pyrrolo[1,2-*a*]quinoxalines **214** (Scheme 72).[209,210] The intermediate 1,4-diketones (**210** or **213**) were isolated from the corresponding 2-furan-amines (**209** or **212**) *via* furan ring-opening. The subsequent treatment with iron in refluxing acetic acid induced the nitro group reduction and intramolecular Paal-Knorr cyclization giving the final products in high yields. The authors demonstrated that it was possible to obtain a diazepine containing a fused thiophene ring **215**, starting from the appropriate furan derivative.[209]



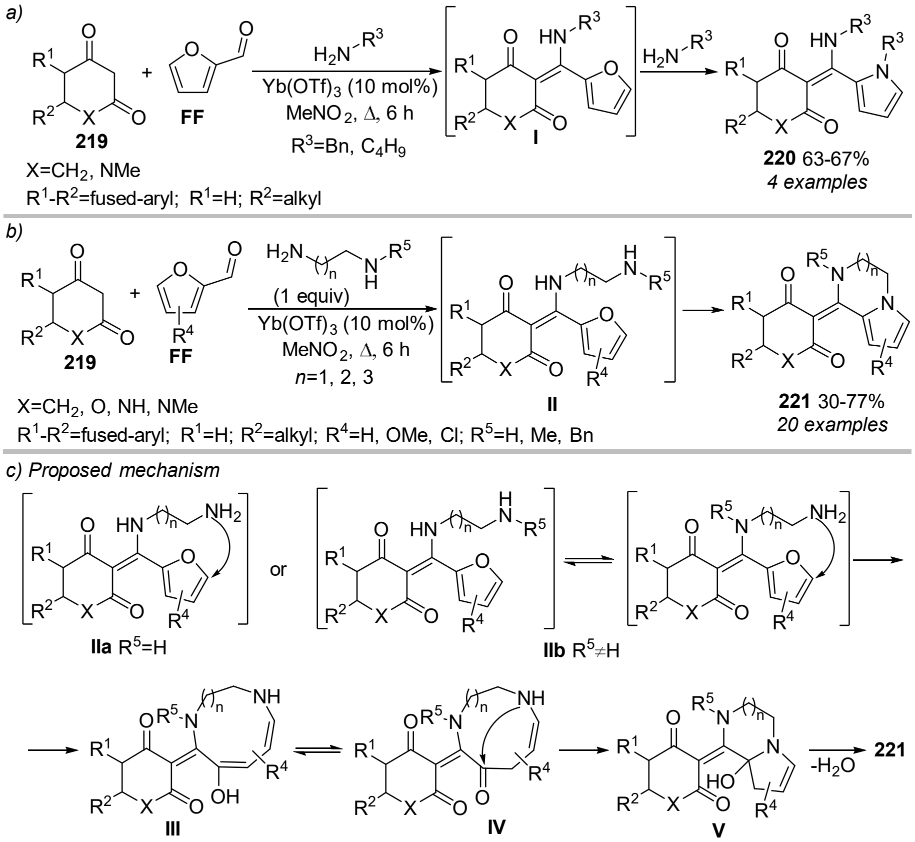
Scheme 72. Synthesis of pyrrolo[1,2-*d*][1,4]diazepines and pyrrolo[1,2-*a*]quinoxalines.

Stroganova and co-workers applied the acid-catalyzed furan ring-opening/recyclization to the synthesis of pyrrolo[1,2-*a*][1,4]diazocines **218** (Scheme 73).[211] In this case, heating a solution of carboxamides **216** in AcOH/HCl, afforded the fused diazocines **218**, through intermediate 1,4-diketones **217**. Intermediates 1,4-diketones **217** could be isolated in high yields when the reaction was carried out at room temperature.



Scheme 73. Synthesis of pyrrolo[1,2-*a*][1,4]diazocines based on furan substrate conversion.

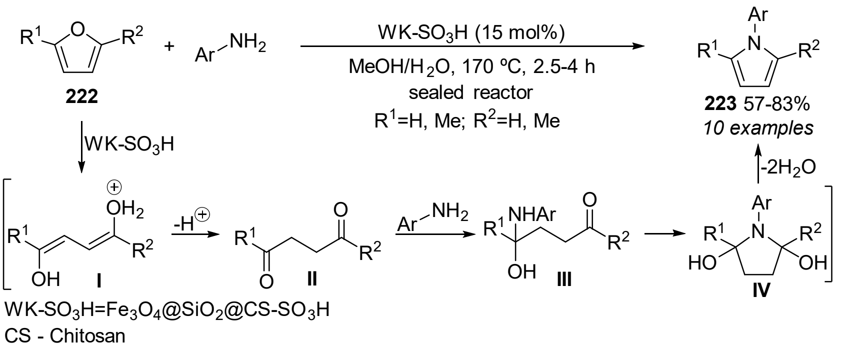
Yang and co-workers developed a multicomponent reaction methodology for the efficient preparation of substituted pyrroles, pyrrolo[1,2-*a*]pyrazines, pyrrolo[1,4]diazepines and pyrrolo[1,4]diazocines based on the acid-catalyzed furan ring-opening (Scheme 74).[212] The multicomponent reaction of 1,3-diketones **219**, furfural (FF) and primary amines, in the presence of catalytic amounts of Yb(OTf)$_3$, gave substituted pyrroles **220** in high yields. Intermediate **I** was formed, which underwent furan ring-opening, followed by the reaction with another molecule of amine, to afford the final product *via* Paal-Knorr cyclization (Scheme 74a). On the other hand, using diamine derivatives under the same reactions conditions, pyrrolo[1,2-*a*]pyrazines **221** (*n*=1), pyrrolo[1,4]diazepines **221** (*n*=2) and pyrrolo[1,4]diazocines **221** (*n*=3) were obtained in good yields (Scheme 74b). The first reaction step is the nitromethane-promoted condensation of 1,3-diketones **219**, substituted furfurals **FF** and diamines giving intermediates **II**. Enols **III** are formed by the nitrogen attack at C5 of the activated furan ring, followed by acid-catalyzed furan ring-opening reaction. The enol-keto tautomerization affords ketones **IV**, which undergo an intramolecular cyclization *via* the nucleophilic attack of the amine nitrogen to the carbonyl carbon giving **V**. The final products are formed by elimination of one molecule of water and aromatization of the pyrrole unit (Scheme 74c).



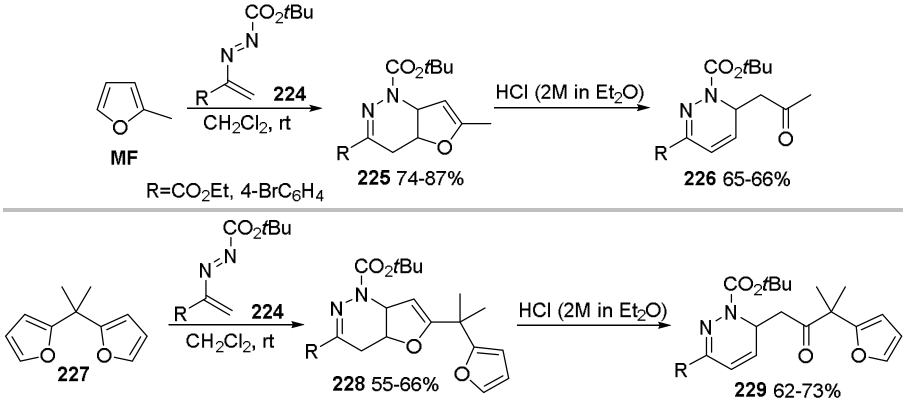
Scheme 74. Acid-catalyzed multicomponent reactions in the synthesis of several heterocyclic systems.

Recently, Li and co-workers developed a novel biocarbon-derived magnetic sulfonic catalyst (WK-SO_3H) for the efficient transformation of furan derivatives into substituted pyrroles (Scheme 75).[213] The major advantage of this catalyst is its easy separation and recovery from the reaction medium by the use of a magnetic field. The reaction of furan derivatives **222** and arylamines afforded the substituted pyrroles **223** in high yields (57-63%). The acid-catalyzed furan ring-opening gave intermediates **I**, which underwent isomerization to diketones **II**. Subsequent amination followed by cyclization and elimination of water gave the final products.

Pinho e Melo and co-workers explored the hetero-Diels-Alder reaction of azoalkenes towards furan derivatives as a way to obtain 1,6-dihydropyridazines (Scheme 76).[214] The reaction of methylfuran (MF) with azoalkenes **224** gave the bicyclic products **225** in high yields (74-87%). Treatment of tetrahydropyridazines **225** with HCl in diethyl ether afforded the 1,6-dihydropyridazines **226** by the acid-promoted furan ring-opening reaction. The structure of derivative **226** (R=CO_2Et) was unambiguously established by X-ray crystallography. Tetrahydro[3,2-*c*]pyridazines **228** were also obtained from the hetero-Diels-Alder reaction of bis(furan-2-yl)-methane **227** with azoalkenes **224**, and the subsequent acid-catalyzed furan ring-opening afforded 1,6-dihydropyridazines **229**, which contains a furan ring.[214] A similar outcome was observed by Gilchrist and co-workers during their studies on base-catalyzed ring-opening of tetrahydropyridazines.[215]



Scheme 75. Synthesis of substituted pyrroles from furan derivatives and arylamines.



Scheme 76. Acid-catalyzed dihydrofuran ring-opening of tetrahydrofuro[3,2-*c*]pyridazines.

6. Conclusion

The quite rich reactivity of furans and 2-hydroxymethylfurans enables them to successfully participate in several transformations that provide an array of functionalized heterocycles, including biologically active compounds, illustrated by the methodologies described in this chapter. The integration of the classical Achmatowicz and Piancatelli rearrangements into cascade reactions has significantly broadened the applicability of these biomass-derived building blocks.

The fast-growing green chemistry research area has been the driving force of important developments on these topics, in particular through the design of highly efficient catalytic systems. Despite the recent progress, more innovative enantioselective methodologies can be expected in the near future to overcome the current challenges.

Acknowledgement

The Coimbra Chemistry Centre - Institute of Molecular Sciences (CQC-IMS) is supported by Fundação para a Ciência e a Tecnologia (FCT) through projects UIDB/00313/2020 and UIDP/00313/2020 (National Funds) and the IMS special complementary funds provided by FCT. Project PTDC/QUI-QOR/0103/2021 was financed by FCT, I.P./MCTES, by national funds (PIDDAC). Terver J. Sase was supported by a PhD grant from Tertiary Education Trust Fund (tetfund), Nigeria.

References

1. Bielski, R.; Grynkiewicz, G. *Green Chem.* **2021**, *23*, 7458-7487.
2. Chen, H.; Wan, K.; Zheng, F.; Zhang, Z.; Zhang, H.; Zhang, Y.; Long, D. *Front. Chem. Eng.* **2021**, *3*, 615309.
3. Zhou, P.; Zhang, Z. *Catal. Sci. Technol.* **2016**, *6*, 3694-3712.
4. Yu, I. K. M.; Tsang, D. C. W. *Bioresour. Technol.* **2017**, *238*, 716-732.
5. Hu, L.; Xu, J.; Zhou, S.; He, A.; Tang, X.; Lin, L.; Xu, J.; Zhao, Y. *ACS Catal.* **2018**, *8*, 2959-2980.
6. Xiong, S.; Guan, Y.; Luo, C.; Zhu, L.; Wang, S. *Energy & Fuels* **2021**, *35*, 14462-14483.
7. Galkin, K. I.; Ananikov, V. P. *ChemistryOpen* **2020**, *9*, 1135-1148.
8. Kucherov, F. A.; Romashov, L. V.; Galkin, K. I.; Ananikov, V. P. *ACS Sustain. Chem. Eng.* **2018**, *6*, 8064-8092.
9. Zhang, J. H.; Wang, T.; Tang, X.; Peng, L. C.; Wei, J. N.; Lin, L. *Bioresources* **2018**, *13*, 7137-7154.
10. Georgiadis, M. P.; Albizati, K. E.; Georgiadis, T. M. *Org. Prep. Proced. Int.* **1992**, *24*, 95-118.
11. Deska, J.; Thiel, D.; Gianolio, E. *Synthesis* **2015**, *47*, 3435-3450.
12. Bielski, R.; Grynkiewicz, G. *Tetrahedron* **2021**, *85*, 132058.
13. Pedro, M.; Tomas, T.; Delso, J. I.; Rosa, M. *Curr. Org. Chem.* **2007**, *11*, 1076-1091.
14. Ghosh, A. K.; Brindisi, M. *RSC Adv.* **2016**, *6*, 111564-111598.
15. Song, W.; Wang, S.; Tang, W. *Chem. Asian J.* **2017**, *12*, 1027-1042.
16. Mahajan, P. S.; Humne, V. T.; Mhaske, S. B. *Curr. Org. Chem.* **2017**, *21*, 503-545.
17. Makarov, A. S.; Uchuskin, M. G.; Trushkov, I. V. *Synthesis* **2018**, *50*, 3059-3086.
18. Zhang, Z.; Han, H.; Wang, L.; Bu, Z.; Xie, Y.; Wang, Q. *Org. Biom. Chem.* **2021**, *19*, 3960-3982.
19. Chen, L.; Li, G.; Zu, L. *Org. Chem. Front.* **2022**, *9*, 5383-5394.
20. van der Pijl, F.; van Delft, F. L.; Rutjes, F. P. J. T. *Eur. J. Org. Chem.* **2015**, *2015*, 4811-4829.
21. Bhandari, Y.; Sajwan, H.; Pandita, P.; Koteswara Rao, V. *Biocatal. Biotransform.* **2022**, *2022*, 1-18.
22. Ciufolini, M. A.; Hermann, C. Y. W.; Dong, Q.; Shimizu, T.; Swaminathan, S.; Xi, N. *Synlett* **1998**, *1998*, 105-114.
23. Ratmanova, N. K.; Andreev, I. A.; Leontiev, A. V.; Momotova, D.; Novoselov, A. M.; Ivanova, O. A.; Trushkov, I. V. *Tetrahedron* **2020**, *76*, 131031.
24. Srivastava, N.; Macha, L.; Ha, H.-J. *Org. Biom. Chem.* **2020**, *18*, 5493-5512.
25. Kandepedu, N.; Abrunhosa-Thomas, I.; Troin, Y. *Org. Chem. Front.* **2017**, *4*, 1655-1704.
26. Fürst, M. C. D.; Sauer, C. S.; Moriyama, T.; Kamimura, A.; Heinrich, M. R. *Eur. J. Org. Chem.* **2016**, *2016*, 3051-3055.
27. Babij, N. R.; Choy, N.; Cismesia, M. A.; Couling, D. J.; Hough, N. M.; Johnson, P. L.; Klosin, J.; Li, X.; Lu, Y.; McCusker, E. O.; Meyer, K. G.; Renga, J. M.; Rogers, R. B.; Stockman, K. E.; Webb, N. J.; Whiteker, G. T.; Zhu, Y. *Green Chem.* **2020**, *22*, 6047-6054.
28. Ferrari, F. D.; Ledgard, A. J.; Marquez, R. *Tetrahedron* **2011**, *67*, 4988-4994.
29. Achmatowicz, O.; Bukowski, P.; Szechner, B.; Zwierzchowska, Z.; Zamojski, A. *Tetrahedron* **1971**, *27*, 1973-1996.
30. Clauson-kaas, N.; Limborg, F.; Fakstorp, J. *Acta Chem. Scand.* **1948**, *2*, 109-115.
31. Cavill, G.; Laing, D.; Williams, P. *Aust. J. Chem.* **1969**, *22*, 2145-2160.
32. Achmatowicz, O.; Grynkiewicz, G.; Szechner, B., *Tetrahedron* **1976**, *32*, 1051-1054.
33. Achmatowicz, O.; Bielski, R. *Carbohydr. Res.* **1977**, *55*, 165-176.
34. McKay, M. J.; Nguyen, H. M. *ACS Catal.* **2012**, *2*, 1563-1595.
35. Weeks, P. D.; Brennan, T. M.; Brannegan, D. P.; Kuhla, D. E.; Elliott, M. L.; Watson, H. A.; Wlodecki, B.; Breitenbach, R. *J. Org. Chem.* **1980**, *45*, 1109-1113.
36. Couladouros, E. A.; Georgiadis, M. P. *J. Org. Chem.* **1986**, *51*, 2725-2727.
37. Ma, Y.; O'Doherty, G. A. *Org. Lett.* **2015**, *17*, 5280-5283.
38. Guo, H.; La Clair, J. J.; Masler, E. P.; O'Doherty, G. A.; Xing, Y. *Tetrahedron* **2016**, *72*, 2280-2286.
39. Aljahdali, A. Z.; Freedman, S. A.; Li, M.; O'Doherty, G. A. *Tetrahedron* **2018**, *74*, 7121-7126.
40. Francisco, K. R.; Li, Y.; Lindquist-Kleissler, B.; Zheng, J.; Xing, Y.; O'Doherty, G. A. *J. CO$_2$ Util.* **2021**, *54*, 101774.
41. Xing, Y.; O'Doherty, G. A. *ChemistrySelect* **2022**, *7*, e202200266.

42. Li, Z.; Ip, F. C. F.; Ip, N. Y.; Tong, R. *Chem. Eur. J.* **2015**, *21*, 11152-11157.
43. Li, Z.; Tong, R. *Synthesis* **2016**, *48*, 1630-1636.
44. Vitellozzi, L.; McAllister, G. D.; Genski, T.; Taylor, R. J. K. *Synthesis* **2016**, *48*, 48-56.
45. Kim, D.-S.; Fang, F. G.; Choi, H.-w.; Fang, H. *Org. Lett.* **2018**, *20*, 4295-4297.
46. Onoue, H.; Marubayashi, R.; Ishikawa, E.; Konoki, K.; Torikai, K.; Ebine, M.; Murata, M.; Oishi, T. *J. Org. Chem.* **2017**, *82*, 9595-9618.
47. Zhang, L.; Zhang, Y.; Li, W.; Qi, X. *Angew. Chem. Int. Ed.* **2019**, *58*, 4988-4991.
48. Zhang, Y.; Zhang, L.; Qi, X. *Synlett* **2020**, *31*, 7-12.
49. Li, Z.; Tong, R. *J. Org. Chem.* **2016**, *81*, 4847-4855.
50. Ghosh, A. K.; Yadav, M. *J. Org. Chem.* **2021**, *86*, 8127-8142.
51. Li, Z.; Tong, R. *J. Org. Chem.* **2017**, *82*, 1127-1135.
52. Singh, P.; Prasad, K. R. *Tetrahedron* **2021**, *84*, 132004.
53. Ghosh, A. K.; Simpson, H. M.; Veitschegger, A. M. *Org. Biom. Chem.* **2018**, *16*, 5979-5986.
54. Ghosh, A. K.; Born, J. R.; Veitschegger, A. M.; Jurica, M. S. *J. Org. Chem.* **2020**, *85*, 8111-8120.
55. Zhao, G.; Canterbury, D. P.; Taylor, A. P.; Cheng, X.; Mikochik, P.; Bagley, S. W.; Tong, R. *Org. Lett.* **2020**, *22*, 458-463.
56. Ma, F.; He, C.; Wang, E.; Tong, R. *Org. Lett.* **2021**, *23*, 6583-6588.
57. Zhao, G.; Tong, R. *Green Chem.* **2019**, *21*, 64-68.
58. Zhao, G.; Tong, R. *Tetrahedron* **2019**, *75*, 1669-1675.
59. Liang, L.; Guo, L.-D.; Tong, R. *Acc. Chem. Res.* **2022**, *55*, 2326-2340.
60. Zhao, G.; Liang, L.; Wang, E.; Tong, R. *ACS Catal.* **2021**, *11*, 3740-3748.
61. Guo, L.-D.; Xu, Z.; Tong, R. *Angew. Chem. Int. Ed.* **2022**, *61*, e202115384.
62. Lefebvre, Y. *Tetrahedron Lett.* **1972**, *13*, 133-136.
63. Laliberte, R.; Medawar, G.; Lefebvre, Y. *J. Med. Chem.* **1973**, *16*, 1084-1089.
64. Koh, P. F.; Loh, T. P. *Green Chem.* **2015**, *17*, 3746-3750.
65. Grabowski, J. P.; Ferrence, G. M.; Mitchell, T. A. *Tetrahedron Lett.* **2020**, *61*, 152324.
66. Ditfe, T.; Bette, E.; N. Sultani, H.; Otto, A.; Wessjohann, L. A.; Arnold, N.; Westermann, B. *Eur. J. Org. Chem.* **2021**, *2021*, 3827-3836.
67. Pham, T. T.; Gözaydın, G.; Söhnel, T.; Yan, N.; Sperry, J. *Eur. J. Org. Chem.* **2019**, *2019*, 1355-1360.
68. Chen, X.; Gao, Y.; Wang, L.; Chen, H.; Yan, N., *ChemPlusChem* **2015**, *80*, 1565-1572.
69. Yu, Z.; Vodanovic-Jankovic, S.; Ledeboer, N.; Huang, S.-X.; Rajski, S. R.; Kron, M.; Shen, B. *Org. Lett.* **2011**, *13*, 2034-2037.
70. Takahashi, K.; Harada, R.; Hoshino, Y.; Kusakabe, T.; Hatakeyama, S.; Kato, K. *Tetrahedron* **2017**, *73*, 3548-3553.
71. van der Pijl, F.; Harmel, R. K.; Richelle, G. J. J.; Janssen, P.; van Delft, F. L.; Rutjes, F. P. J. T., *Org. Lett.* **2014**, *16*, 2038-2041.
72. Ren, J.; Wang, J.; Tong, R. *Org. Lett.* **2015**, *17*, 744-747.
73. Maitra, S.; Bodugam, M.; Javed, S.; Hanson, P. R. *Org. Lett.* **2016**, *18*, 3094-3097.
74. Peng, H.; Luo, W.; Jiang, H.; Yin, B. *J. Org. Chem.* **2018**, *83*, 12869-12879.
75. Virieux, D.; Delogu, F.; Porcheddu, A.; García, F.; Colacino, E. *J. Org. Chem.* **2021**, *86*, 13885-13894.
76. Falenczyk, C.; Pölloth, B.; Hilgers, P.; König, B. *Synth. Commun.* **2015**, *45*, 348-354.
77. Ho, T.-L.; Sapp, S. G. *Synth. Commun.* **1983**, *13*, 207-211.
78. Ji, Y.; Benkovics, T.; Beutner, G. L.; Sfouggatakis, C.; Eastgate, M. D.; Blackmond, D. G. *J. Org. Chem.* **2015**, *80*, 1696-1702.
79. Henderson, J. A.; Jackson, K. L.; Phillips, A. J. *Org. Lett.* **2007**, *9*, 5299-5302.
80. Ghosh, A. K.; Chen, Z.-H. *Org. Lett.* **2013**, *15*, 5088-5091.
81. Márquez-Cadena, M. A.; Zhang, W.; Tong, R. *Org. Lett.* **2021**, *23*, 9227-9231.
82. Chen, J.; Jiang, Z.; Fukuzumi, S.; Nam, W.; Wang, B. *Coord. Chem. Rev.* **2020**, *421*, 213443.
83. Xing, Q.; Hao, Z.; Hou, J.; Li, G.; Gao, Z.; Gou, J.; Li, C.; Yu, B. *J. Org. Chem.* **2021**, *86*, 9563-9586.
84. Piancantelli, G.; Scettri, A.; Barbadoro, S. *Tetrahedron Lett.* **1976**, *39*, 3555-3558.
85. Piancantelli, G.; Scettri, A. *Tetrahedron* **1977**, *33*, 69-72.
86. Piancantelli, G.; D'Auria, M.; D'Onofrio, F. *Synthesis* **1994**, *1994*, 867-889.

87. Shen, G.; Andrioletti, B.; Queneau, Y. *Curr. Opin. Green Sustain. Chem.* **2020**, *26*, 100384.
88. Weigang, F.; Charlie, V.; Yves, Q.; Florence, P. *Curr. Org. Synth.* **2019**, *16*, 583-614.
89. Piutti, C.; Quartieri, F. *Molecules* **2013**, *18*, 12290-12312.
90. Verrier, C.; Moebs-Sanchez, S.; Queneau, Y.; Popowycz, F. *Org. Biom. Chem.* **2018**, *16*, 676-687.
91. Zhong, S.; Xu, L.; Cai, Y. *Synthesis* **2022**, *54*, 589-599.
92. Palframan, M. J.; Pattenden, G. *Chem. Commun.* **2014**, *50*, 7223-7242.
93. Scettri, A.; Piancantelli, G.; D'Auria, M.; David, G. *Tetrahedron* **1979**, *35*, 135-138.
94. Faza, O. N.; Lopez, C. S.; Alvarez, R.; de Lera, A. R. *Chem. Eur. J.* **2004**, *10*, 4324-4333.
95. Wenz, D. R.; Read de Alaniz, J. *Eur. J. Org. Chem.* **2015**, *2015*, 23-37.
96. Kalidindi, S.; Jeong, W. B.; Schall, A.; Bandichhor, R.; Nosse, B.; Reiser, O. *Angew. Chem. Int. Ed.* **2007**, *46*, 6361-6363.
97. Dobler, D.; Reiser, O. *J. Org. Chem.* **2016**, *81*, 10357-10365.
98. Song, L.; Yao, H.; Zhu, L.; Tong, R. *Org. Lett.* **2013**, *15*, 6-9.
99. Katsuta, R.; Aoki, K.; Yajima, A.; Nukada, T. *Tetrahedron Lett.* **2013**, *54*, 347-350.
100. Arisetti, N.; Reiser, O. *Org. Lett.* **2015**, *17*, 94-97.
101. Kumaraguru, T.; Babita, P.; Sheelu, G.; Lavanya, K.; Fadnavis, N. W. *Org. Process Res. Dev.* **2013**, *17*, 1526-1530.
102. Henschke, J. P.; Liu, Y.; Huang, X.; Chen, Y.; Meng, D.; Xia, L.; Wei, X.; Xie, A.; Li, D.; Huang, Q.; Sun, T.; Wang, J.; Gu, X.; Huang, X.; Wang, L.; Xiao, J.; Qiu, S. *Org. Proc. Res. Dev.* **2012**, *16*, 1905-1916.
103. Reiser, O.; Ulbrich, K.; Kreitmeier, P. *Synlett* **2010**, *2010*, 2037-2040.
104. Fisher, D.; Palmer, L. I.; Cook, J. E.; Davis, J. E.; Read de Alaniz, J. *Tetrahedron* **2014**, *70*, 4105-4110.
105. Cacheux, F.; Le Goff, G.; Ouazzani, J.; Bignon, J.; Retailleau, P.; Marinetti, A.; Voituriez, A.; Betzer, J.-F. *Org. Chem. Front.* **2021**, *8*, 2449-2455.
106. Read de Alaniz, J.; Palmer, L. I. *Org. Lett.* **2013**, *15*, 476-479.
107. Read de Alaniz, J.; Palmer, L. I. *Synlett* **2014**, *25*, 8-11.
108. Schober, L.; Sako, M.; Takizawa, S.; Gröger, H.; Sasai, H. *Chem. Commun.* **2020**, *56*, 10151-10154.
109. Yin, B.; Huang, L.; Wang, X.; Liu, J.; Jiang, H. *Adv. Synth. Catal.* **2013**, *355*, 370-376.
110. Huang, L.; Zhang, X.; Li, J.; Ding, K.; Li, X.; Zheng, W.; Yin, B. *Eur. J. Org. Chem.* **2014**, *2014*, 338-349.
111. Solanke, P. R.; Cinsani, R.; Nayani, K.; Mainkar, P. S.; Chandrasekhar, S. *Chem. Commun.* **2022**, *58*, 5530-5533.
112. Veits, G. K.; Wenz, D. R.; Read de Alaniz, J. *Angew. Chem. Int. Ed.* **2010**, *49*, 9484-9487.
113. Marin, L.; Force, G.; Gandon, V.; Schulz, E.; Lebœuf, D. *Eur. J. Org. Chem.* **2020**, *2020*, 5323-5328.
114. Palmer, L. I.; de Alaniz, J. R. *Angew. Chem. Int. Ed.* **2011**, *50*, 7167-7170.
115. Yu, D.; Thai, V. T.; Palmer, L. I.; Veits, G. K.; Cook, J. E.; de Alaniz, J. R.; Hein, J. E. *J. Org. Chem.* **2013**, *78*, 12784-12789.
116. Xu, L.; Yang, Q.; Zhong, S.; Li, H.; Tang, Y.; Cai, Y. *Org. Lett.* **2020**, *22*, 9016-9021.
117. Subba Reddy, B. V.; Vikram Reddy, Y.; Singarapu, K. K. *Org. Biom. Chem.* **2016**, *14*, 1111-1116.
118. Gouse, S.; Reddy, N. R.; Baskaran, S. *Org. Lett.* **2019**, *21*, 3822-3827.
119. Nunes, J. P. M.; Afonso, C. A. M.; Caddick, S. *RSC Adv.* **2013**, *3*, 14975-14978.
120. Leboeuf, D.; Schulz, E.; Gandon, V. *Org. Lett.* **2014**, *16*, 6464-6467.
121. Leboeuf, D.; Marin, L.; Michelet, B.; Perez-Luna, A.; Guillot, R.; Schulz, E.; Gandon, V. *Chem. Eur. J.* **2016**, *22*, 16165-16171.
122. Marin, L.; Guillot, R.; Gandon, V.; Schulz, E.; Lebœuf, D. *Org. Chem. Front.* **2018**, *5*, 640-647.
123. Baldé, B.; Force, G.; Marin, L.; Guillot, R.; Schulz, E.; Gandon, V.; Lebœuf, D. *Org. Lett.* **2018**, *20*, 7405-7409.
124. Wang, S.; Guillot, R.; Carpentier, J. F.; Sarazin, Y.; Bour, C.; Gandon, V.; Leboeuf, D. *Angew. Chem. Int. Ed.* **2020**, *59*, 1134-1138.
125. Tang, W.-B.; Cao, K.-S.; Meng, S.-S.; Zheng, W.-H. *Synthesis* **2017**, *49*, 3670-3675.
126. Pramanik, S.; Jagadeesh, C.; Chatterjee, A.; Debnath, S. C.; Saha, J. *Org. Biomol. Chem.* **2022**, *20*, 5249-5253.

127. Cai, Y.; Tang, Y.; Atodiresei, I.; Rueping, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 14126-14130.
128. Li, H.; Tong, R.; Sun, J. *Angew. Chem. Int. Ed.* **2016**, *55*, 15125-15128.
129. Gade, A. B.; Patil, N. T. *Synlett* **2017**, *28*, 1096-1100.
130. Marin, L.; Jerhaoui, S.; Kolodziej, E.; Guillot, R.; Gandon, V.; Colobert, F.; Schulz, E.; Wencel-Delord, J.; Lebœuf, D. *Adv. Synth. Catal.* **2021**, *363*, 4277-4282.
131. Pellissier, H. *Org. Prep. Proced. Int.* **2019**, *51*, 311-344.
132. Reddy, B. V. S.; Reddy, Y. V.; Lakshumma, P. S.; Narasimhulu, G.; Yadav, J. S.; Sridhar, B.; Reddy, P. P.; Kunwar, A. C. *RSC Adv.* **2012**, *2*, 10661-10666.
133. Liu, J.; Shen, Q.; Yu, J.; Zhu, M.; Han, J.; Wang, L. *Eur. J. Org. Chem.* **2012**, *2012*, 6933-6939.
134. Nayani, K.; Cinsani, R.; Hussaini A. S. D.; Mainkar, P. S.; Chandrasekhar, S. *Eur. J. Org. Chem.* **2017**, *2017*, 5671-5678.
135. Vonteddu, N. R.; Solanke, P. R.; Nayani, K.; Chandrasekhar, S. *Org. Lett.* **2020**, *22*, 8555-8560.
136. Wei, Z.; Zhang, J.; Yang, H.; Jiang, G. *Org. Lett.* **2019**, *21*, 2790-2794.
137. Went, D. R.; Read de Alaniz, J. *Org. Lett.* **2013**, *15*, 3250-3253.
138. Lewis, K. G.; Mulquiney, C. E., *Aust. J. Chem.* **1979**, *32*, 1079-1092.
139. Li, S. W.; Batey, R. A. *Chem. Commun.* **2007**, 3759-3761.
140. Duspara, P. A.; Batey, R. A. *Angew. Chem. Int. Ed.* **2013**, *52*, 10862-10866.
141. Ramesh, D.; Reddy, T. S.; Narasimhulu, M.; Rajaram, S.; Suryakiran, N.; Mahesh, K. C.; Venkateswarlu, Y. *Chem. Lett.* **2009**, *38*, 586-587.
142. Gomes, R. F. A.; Esteves, N. R.; Coelho, J. A. S.; Afonso, C. A. M. *J. Org. Chem.* **2018**, *83*, 7509-7513.
143. Procopio, A.; Costanzo, P.; Curini, M.; Nardi, M.; Oliverio, M.; Sindona, G. *ACS Sustainable Chem. Eng.* **2013**, *1*, 541-544.
144. Estevão, M. S.; Afonso, C. A. M. *Tetrahedron Lett.* **2017**, *58*, 302-304.
145. Wang, L.; Yu, J.; Liu, J.; Zhu, M.; Li, J.; Zheng, X. *Synthesis* **2013**, *45*, 2165-2170.
146. Nardi, M.; Costanzo, P.; De Nino, A.; Di Gioia, M. L.; Olivito, F.; Sindona, G.; Procopio, A. *Green Chem.* **2017**, *19*, 5403-5411.
147. Griffiths, K.; Gallop, C. W.; Abdul-Sada, A.; Vargas, A.; Navarro, O.; Kostakis, G. E. *Chem. Eur. J.* **2015**, *21*, 6358-6361.
148. Griffiths, K.; Kumar, P.; Mattock, J. D.; Abdul-Sada, A.; Pitak, M. B.; Coles, S. J.; Navarro, O.; Vargas, A.; Kostakis, G. E. *Inorg. Chem.* **2016**, *55*, 6988-6994.
149. Stenhouse, J. *Liebigs Ann.* **1850**, *74*, 278-297.
150. Gomes, R. F. A.; Coelho, J. A. S.; Afonso, C. A. M. *Chem. Eur. J.* **2018**, *24*, 9170-9186.
151. Sampani, S. I.; McGown, A.; Vargas, A.; Abdul-Sada, A.; Tizzard, G. J.; Coles, S. J.; Spencer, J.; Kostakis, G. E. *J. Org. Chem.* **2019**, *84*, 6858-6867.
152. Xu, L.; Li, H.; Xing, L.; Yang, Q.; Tang, Y.; Cai, Y. *J. Org. Chem.* **2022**, *87*, 855-865.
153. Xu, L.; Zhong, S.; Yang, Q.; Wei, J.; Zou, J.; Li, H.; Cai, Y. *ACS Catal.* **2021**, *11*, 10198-10207.
154. Messori, A.; Fasolini, A.; Mazzoni, R. *ChemSusChem* **2022**, *15*, e202200228.
155. Li, X.; Jia, P.; Wang, T. *ACS Catal.* **2016**, *6*, 7621-7640.
156. Liu, B.; Zhang, Z. *ACS Catal.* **2015**, *6*, 326-338.
157. Gupta, K.; Rai, R. K.; Singh, S. K. *ChemCatChem* **2018**, *10*, 2326-2349.
158. Huang, Z.; Wang, J.; Lei, J.; Zhao, W.; Chen, H.; Yang, Y.; Xu, Q.; Liu, X. *Front. Chem.* **2022**, *10*, 925603.
159. Turkin, A. A.; Makshina, E. V.; Sels, B. F. *Chemsuschem* **2022**, *15*, e202200412.
160. Jin, X.; Yin, B.; Xia, Q.; Fang, T.; Shen, J.; Kuang, L.; Yang, C. *ChemSusChem* **2019**, *12*, 71-92.
161. Fang, W.; Riisager, A. *Green Chem.* **2021**, *23*, 670-688.
162. Chatterjee, M.; Ishizaka, T.; Kawanami, H. *Green Chem.* **2014**, *16*, 1543-1551.
163. Saha, B.; Bohn, C. M.; Abu-Omar, M. M. *ChemSusChem* **2014**, *7*, 3095-101.
164. Hu, L.; Tang, X.; Xu, J.; Wu, Z.; Lin, L.; Liu, S. *Ind. Eng. Chem. Res.* **2014**, *53*, 3056-3064.
165. Fulignati, S.; Antonetti, C.; Licursi, D.; Pieraccioni, M.; Wilbers, E.; Heeres, H. J.; Raspolli Galletti, A. M. *Appl. Catal. A* **2019**, *578*, 122-133.
166. Sun, G.; An, J.; Hu, H.; Li, C.; Zuo, S.; Xia, H. *Catal. Sci. Tech.* **2019**, *9*, 1238-1244.
167. Duan, Y.; Zheng, M.; Li, D. M.; Deng, D. S.; Ma, L. F.; Yang, Y. L. *Green Chem.* **2017**, *19*, 5103-5113.

168. Xu, Z.; Yan, P.; Xu, W.; Liu, X.; Xia, Z.; Chung, B.; Jia, S.; Zhang, Z. C. *ACS Catal.* **2015**, *5*, 788-792.
169. Yang, Y. L.; Xie, Y. F.; Deng, D. S.; Li, D. M.; Zheng, M.; Duan, Y. *Chemistryselect* **2019**, *4*, 11165-11171.
170. Yang, Y. L.; Yang, D. X.; Zhang, C.; Zheng, M.; Duan, Y. *Molecules* **2020**, *25*, 2475.
171. Zhang, C.; Li, Y. J.; Lv, X. C.; Gao, X. H.; Duan, Y.; Sui, D.; Yang, Y. L. *Chemistryselect* **2022**, *7*, e202103797.
172. Buntara, T.; Noel, S.; Phua, P. H.; Melian-Cabrera, I.; de Vries, J. G.; Heeres, H. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 7083-7087.
173. Wozniak, B.; Spannenberg, A.; Li, Y.; Hinze, S.; de Vries, J. G. *ChemSusChem* **2018**, *11*, 356-359.
174. Ramos, R.; Grigoropoulos, A.; Griffiths, B.; Katsoulidis, A. P.; Zanella, M.; Manning, T. D.; Blanc, F.; Claridge, J. B.; Rosseinsky, M. J. *J. Catal.* **2019**, *375*, 224-233.
175. Rodriguez-Padron, D.; Perosa, A.; Longo, L.; Luque, R.; Selva, M. *ChemSusChem* **2022**, *15*, e202200503.
176. Liang, X.; Haynes, B. S.; Montoya, A. *Energy & Fuels* **2017**, *32*, 4139-4148.
177. Pileidis, F. D.; Titirici, M. M. *ChemSusChem* **2016**, *9*, 562-82.
178. Ren, D.; Song, Z.; Li, L.; Liu, Y.; Jin, F.; Huo, Z. *Green Chem.* **2016**, *18*, 3075-3081.
179. Tong, Z. K.; Li, X.; Zhu, J. W.; Chen, S. X.; Dai, G. P.; Deng, Q.; Wang, J.; Yang, W. R.; Zeng, Z. L.; Zou, J. J. *Chemsuschem* **2021,** e202102444.
180. Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKervey, M. A. *Chem. Rev.* **2015**, *115*, 9981-10080.
181. Soam, P.; Kamboj, P.; Tyagi, V. *Asian J. Org. Chem.* **2022**, *11*, e202100570.
182. Muthusamy, S.; Azhagan, D. *Tetrahedron Lett.* **2011**, *52*, 6732-6735.
183. Muthusarny, S.; Balasubramani, A.; Suresh, E. *Tetrahedron* **2016**, *72*, 1749-1757.
184. Parr, B. T.; Green, S. A.; Davies, H. M. *J. Am. Chem. Soc.* **2013**, *135*, 4716-8.
185. Funakoshi, Y.; Miura, T.; Murakami, M. *Org. Lett.* **2016**, *18*, 6284-6287.
186. Makarov, A. S.; Uchuskin, M. G.; Hashmi, A. S. K. *Chem. Sci.* **2019**, *10*, 8583-8588.
187. Nejrotti, S.; Prandi, C. *Synthesis* **2021**, *53*, 1046-1060.
188. Zeng, Z.; Jin, H.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem. Int. Ed. Engl.* **2018**, *57*, 16549-16553.
189. Du, X. C.; Yu, J. F.; Gong, J.; Zaman, M.; Pereshivko, O. P.; Peshkov, V. A. *Eur. J. Org. Chem.* **2019**, *2019*, 2502-2507.
190. Nejrotti, S.; Marra, F.; Priola, E.; Maranzana, A.; Prandi, C. *J. Org. Chem.* **2021**, *86*, 8295-8307.
191. Pirovano, V.; Brambilla, E.; Rizzato, S.; Abbiati, G.; Bozzi, M.; Rossi, E. *J. Org. Chem.* **2019**, *84*, 5150-5166.
192. Trushkov, I. V.; Uchuskin, M. G.; Butin, A. V. *Eur. J. Org. Chem.* **2015**, *2015*, 2999-3016.
193. Abaev, V. T.; Trushkov, I. V.; Uchuskin, M. G. *Chem. Heterocycl. Compd.* **2016**, *52*, 973-995.
194. Butin, A. V.; Zavodnik, V. E.; Kul'nevich, V. G. *Chem. Heterocycl. Compd.* **1992**, *28*, 835-836.
195. Butin, A. V.; Krapivin, G. D.; Zavodnik, V. E.; Kul'nevich, V. G. *Chem. Heterocycl. Compd.* **1993**, *29*, 524-533.
196. Makarov, A. S.; Kekhvaeva, A. E.; Chalikidi, P. N.; Abaev, V. T.; Trushkov, I. V.; Uchuskin, M. G. *Synthesis* **2019**, *51*, 3747-3757.
197. Shelke, Y. G.; Hande, P. E.; Gharpure, S. J. *Org. Biom. Chem.* **2021**, *19*, 7544-7574.
198. Butin, A. V.; Smirnov, S. K. *Tetrahedron Lett.* **2005**, *46*, 8443-8445.
199. Butin, A. V.; Smirnov, S. K.; Stroganova, T. A.; Bender, W.; Krapivin, G. D. *Tetrahedron* **2007**, *63*, 474-491.
200. Kuznetsov, A.; Makarov, A.; Rubtsov, A. E.; Butin, A. V.; Gevorgyan, V. *J. Org. Chem.* **2013**, *78*, 12144-12153.
201. Faragher, R.; Gilchrist, T. L. *J. Chem. Soc. Perkin Trans. 1* **1979**, 258-262.
202. Lopes, S. M. M.; Cardoso, A. L.; Lemos, A.; Pinho e Melo, T. M. V. D. *Chem. Rev.* **2018**, *118*, 11324-11352.
203. Alves, A. J. S.; Lopes, S. M. M.; Henriques, M. S. C.; Paixao, J. A.; Pinho e Melo, T. M. V. D. *Eur. J. Org. Chem.* **2017**, *2017*, 4011-4025.

204. Sawengngen, N.; Chalikidi, P. N.; Araby, S.; Hampel, F.; Gmeiner, P.; Serdyuk, O. V. *Org. Biom. Chem.* **2019**, *17*, 4850-4855.
205. Makarov, A. S.; Merkushev, A. A.; Uchuskin, M. G.; Trushkov, I. V. *Org. Lett.* **2016**, *18*, 2192-2195.
206. Merkushev, A. A.; Makarov, A. S.; Shpuntov, P. M.; Abaev, V. T.; Trushkov, I. V.; Uchuskin, M. G. *Eur. J. Org. Chem.* **2021**, *2021*, 1274-1285.
207. Serdyuk, O. V.; Hampel, F.; Abaev, V. T. *Chem. Heterocycl. Compd.* **2020**, *56*, 1477-1484.
208. Zelina, E. Y.; Nevolina, T. A.; Sorotskaja, L. N.; Skvortsov, D. A.; Trushkov, I. V.; Uchuskin, M. G. *J. Org. Chem.* **2018**, *83*, 11747-11757.
209. Zelina, E. Y.; Nevolina, T. A.; Skvortsov, D. A.; Trushkov, I. V.; Uchuskin, M. G. *J. Org. Chem.* **2019**, *84*, 13707-13720.
210. Zelina, E. Y.; Nevolina, T. A.; Sorotskaja, L. N.; Skvortsov, D. A.; Trushkov, I. V.; Uchuskin, M. G. *Tetrahedron Lett.* **2020**, *61*, 151532.
211. Stroganova, T. A.; Vasilin, V. K.; Krapivin, G. D. *Synlett* **2016**, *27*, 1569-1571.
212. Chithanna, S.; Yang, D.-Y. *J. Org. Chem.* **2019**, *84*, 1339-1347.
213. Wang, K.; Wu, M.; Liu, Y.; Yang, Y.; Li, H. *New J. Chem.* **2022**, *46*, 5312-5320.
214. Lopes, S. M. M.; Henriques, M. S. C.; Paixao, J. A.; Pinho e Melo, T. M. V. D. *Eur. J. Org. Chem.* **2015**, *2015*, 6146-6151.
215. Gilchrist, T. L.; Hughes, D.; Stretch, W.; Chrystal, E. J. T. *J. Chem. Soc. Perkin Trans. 1* **1987**, 2505-2509.