UNICA UNIVERSITÀ DEGLI STUDI DI CAGLIARI

The Heyns Rearrangement: Synthetic Routes Beyond Carbohydrate Chemistry

Stefano Barranco, [a] Federico Cuccu, [a] Mauro Uras, [a] and Angelo Frongia*[a]

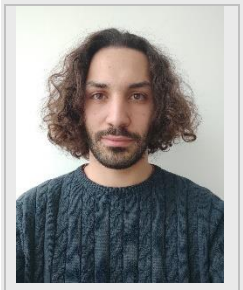
[a] S. Barranco, F. Cuccu, M. Uras, Prof. Dr. A. Frongia
Dipartimento di Scienze Chimiche e Geologiche
Università degli Studi di Cagliari
Complesso Universitario di Monserrato, S.S. 554, Bivio per Sestu, I-09042, Monserrato, Cagliari, Italy. Fax: (+39)-070-675-4388; phone: (+39)-070-675-4406. E-mail: afrongia@unica.it
https://web.unica.it/unica/page/it/angelo_frongia

Abstract: This concept review describes the recent achievements on the Heyns rearrangement appeared in literature over the last decade and aims to provide the reader with a general overview of the fundamental synthetic advances in this research area.

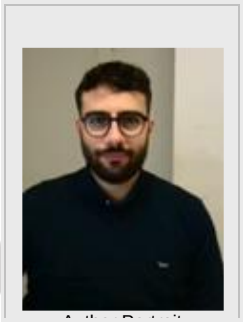
1. Introduction

The Amadori- and Heyns rearrangements are chemical reactions that occur between a reducing sugars and suitable amines by acid or base catalysis,[1] resulting in the generation of a Schiff base. Going through a sequence of rearrangements, this intermediate ultimately give rise to a stable α-amino carbonyl adduct, which is a key component in the Maillard reaction.[2] Specifically, Amadori rearrangement products are typical for a Schiff base derived from aldose sugar, whereas Heyns rearrangement products derive essentially from ketose ones. They are important reactions in food chemistry as they are responsible for the development of flavors and aromas in various cooked foods, including but not limited to bread, roasted coffee, and grilled meat.[3] Additionally, Amadori- and Heyns reactions have implications in the fields of biochemistry and medicine.[4] Being involved in the formation of advanced glycation end products (AGEs), they are known to play a role in numerous age-related diseases, including diabetes, Alzheimer's disease, cardiovascular disorders, and cancer.

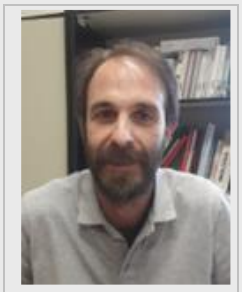
Stefano Barranco graduated in 2020 in Chemistry and Pharmaceutical Technologies at the University of Cagliari. He is currently pursuing doctoral research under the guidance of Prof. Angelo Frongia. His research interest focusses on synthetic methodologies for the chemo- and stereoselective functionalization of substituted cyclobutanes.



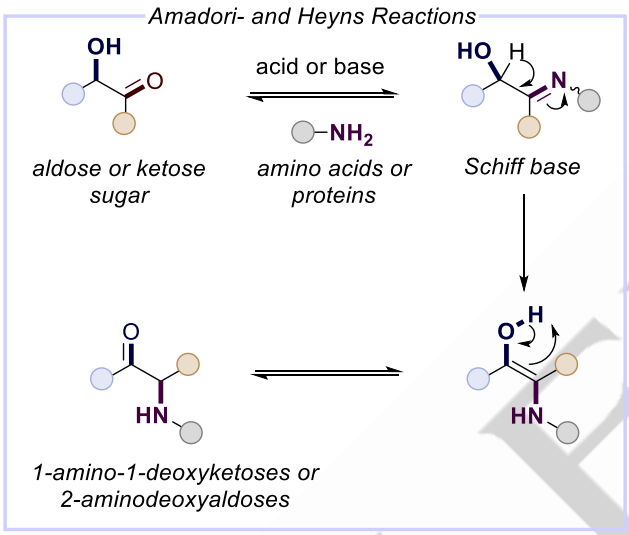
Federico Cuccu graduated. in 2020 in Chemistry and Pharmaceutical Technologies at the University of Cagliari, under the supervision of prof. Angelo Frongia. He worked on strained carbocycles, tandem reactions and rearrangements. He is currently a PhD candidate in mechanochemistry and sustainable chemistry at the University of Cagliari, under prof. Andrea Porcheddu's guidance. In 2022, he was visiting scientist at the University College of London, working in the field of mechanochemistry and enabling technologies under the supervision of prof. Duncan Browne. His current research interest mainly centres around solid state amidation, oxidation, and hydrogenation reactions, as well as solvent-free heterocycle synthesis.



Mauro Uras graduated in 2023 in Pharmacy at the University of Cagliari. He is currently a Ph.D. candidate at the University of Cagliari under the supervision of Prof. Angelo Frongia. His research interests focus on asymmetric organocatalysis and development of new synthetic methodologies.



Angelo Frongia received his PhD degree in Chemistry from the University of Cagliari under the supervision of Prof. P. P. Piras. In 2001, he joined Dr. Jacques Salaün at the Laboratoire des Carbocycles (CNRS) Paris, France as a postdoctoral fellow. Then he completed internships within the group of Prof. Piras at the University of Cagliari (2002-2008) and following post-doctoral research (2009) in the group of Prof. D. J. Aitken at ICMMO, University Paris Sud, France, he started his independent career at University of Cagliari in 2010. His research interests focus on the synthesis and reactivity of strained carbocycles and organocatalysis.

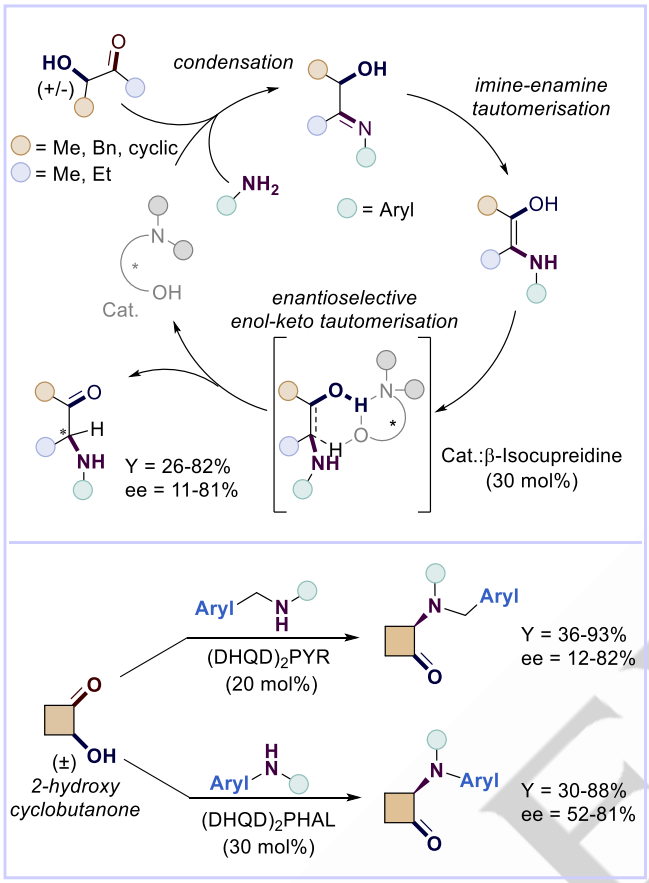


Scheme 1. General reaction mechanism for the Amadori- and Heyns rearrangements.

Though predominantly explored in carbohydrates and food chemistry, Amadori- and Heyns rearrangements, often underrated in their synthetic utility, present intriguing and untapped opportunities for organic chemists. However, the recent years have witnessed a renewed interest in Heyns rearrangement, and some advancements in organic synthesis have paved the way for increased research in this area. A few reviews have been published so far which aim to summarize the progress made in this field but from different perspectives.[5] In this concept review, our objective is to provide an overview of recent advances in Heyns rearrangement that goes beyond the carbohydrate and food chemistry. It is worth noting that these latest findings enable efficient access to optically active α-amino ketones, relevant structural motifs in bioactive molecules and natural products. Furthermore, successes in the synthesis of complex heterocycles such as pyrrole, indole, quinoxaline, 1,2-dihydronaphthofurans, 2,3-dihydropyrazines, hydantoins, among others, by means of novel tandem reactions based on Heyns rearrangement, have further demonstrated the potential of this rearrangement in organic synthesis. Finally, the very recent discovery based on *in-situ* trapping of the transient amino enol intermediate with a suitable electrophile as well as the development of the Heyns rearrangement without the shift of the carbonyl group may unlock new reaction pathways and enable the synthesis of previously inaccessible compounds. We organized the content of this concept review into four main sections, allowing for a thorough description of the above-mentioned new achievements: 1) catalytic enantioselective Heyns rearrangements; 2) one-pot tandem reactions based on Heyns rearrangement; 3) interrupted Heyns rearrangements and 4) consecutive Heyns rearrangements.

2. Catalytic Enantioselective Heyns Rearrangements

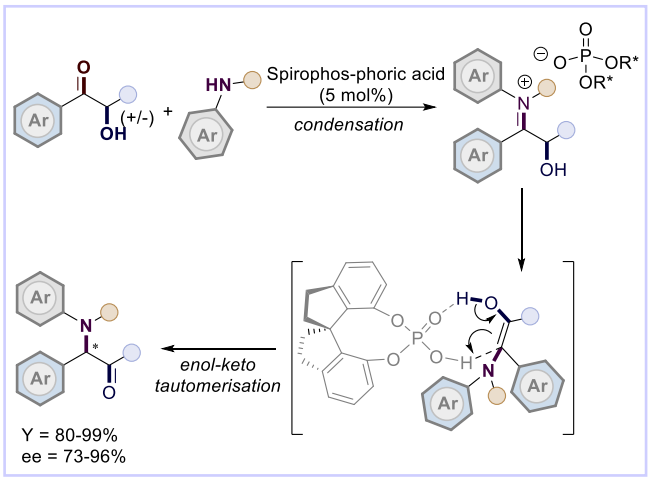
In 2013, we disclosed a new strategy for the enantioselective synthesis of optically active α-amino ketones starting from simple racemic α-hydroxyketones and primary arylamines in the presence of catalytic amount of β-isocupreidine.[6] The products have been isolated in good to high yield and ee up to 81%. The transformation proceeded via tandem condensation-enantioselective keto-enol tautomerization process reminiscent of the Heyns rearrangement. This work constituted the first catalytic asymmetric Heyns rearrangement (Scheme 2).



Scheme 2. Enantioselective Heyns rearrangement catalyzed by *Cinchona* alkaloids. Reproduced from ref. [6] Copyright (2013), with permission from Royal Society of Chemistry (top). Reproduced from ref. [7] Copyright (2014, 1015), with permission from Wiley-VCH (bottom).

Then, we applied the same concept to the synthesis of several intriguing optically active 2-aminocyclobutanones. Using a selection of *N*-alkyl anilines and *N*-alkyl benzylamines in reaction with α-hydroxycyclobutanone, commercially available $(DHQD)_2PHAL$ and $(DHQD)_2PYR$ were found to be the best catalysts, providing the corresponding α-aminocyclobutanone with ee up to 82%.[7]

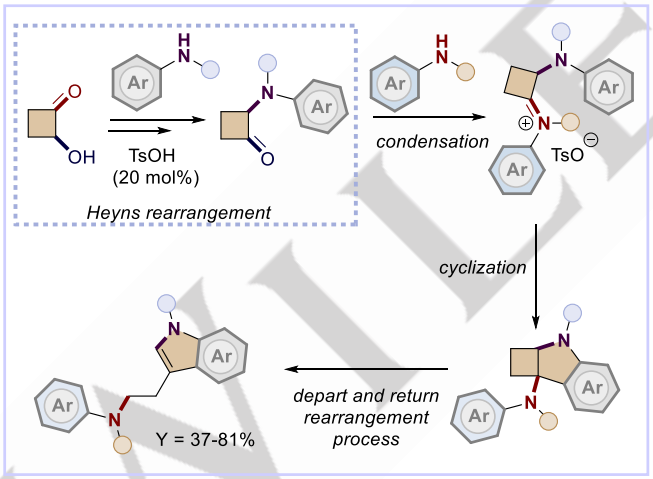
Later after these works, in 2022, an enantioselective Brønsted acid catalyzed Heyns rearrangement reaction was explored by Zhu et al. A broad spectrum of α-hydroxy aromatic ketones with variously substituted phenyl groups effectively and stereoselectively reacted with aromatic amines, under mild reaction conditions, to deliver the corresponding chiral α-aryl-α-aminoketone in high yields and with high to excellent enantioselectivities. Their mechanistic investigation found that the transformation might proceed through an *in-situ* generation of an 1,2-enaminol intermediate followed by a Brønsted acid promoted asymmetric proton-transfer reaction (Scheme 3).[8]



Scheme 3. Enantioselective Brønsted acid catalyzed Heyns rearrangement. Reproduced from ref. [8] Copyright (2022), with permission from Wiley-VCH.

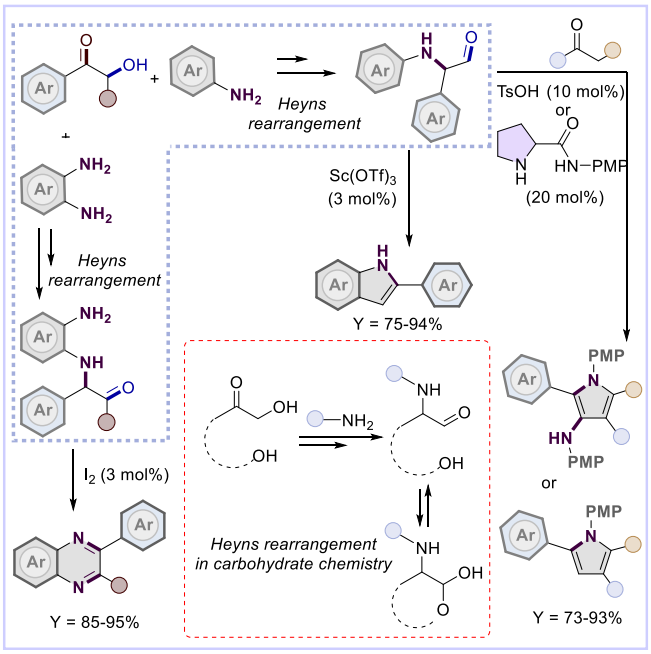
3. One-Pot Tandem Reactions Based on Heyns Rearrangement

Recently, the Heyns rearrangement has found broad utility in the synthesis of a range of heteroaromatic scaffolds with specific substitution patterns and functional groups. This was accomplished by designing novel tandem reactions where the Heyns rearrangement product serves as the key transient synthetic intermediate. In this regard, in 2015, during our studies on Heyns rearrangement, we stumbled upon an interestingly discovery. The reaction between α-hydroxycyclobutanone and two equivalents of a secondary aniline, in the presence of a Brønsted acid catalyst, results in the formation of the tryptamine core via tandem Heyns rearrangement-ring closure-ring fission process ("depart-and-return" rearrangement process).[9] Through this strategy, we were able to access a variety of densely functionalized tryptamines with various ring-substituent patterns in moderate to good yields (Scheme 4).



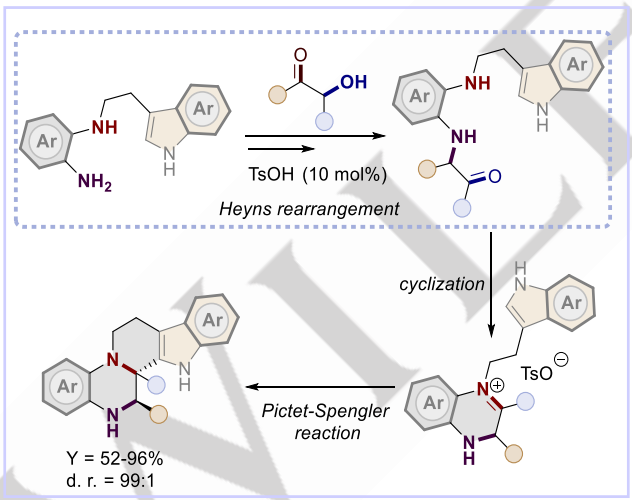
Scheme 4. Synthesis of functionalized tryptamines by Brønsted acid catalyzed cascade reactions based on Heyns rearrangement. Reproduced from ref. [9] Copyright (2015), with permission from Royal Society of Chemistry.

In this context, in 2016, Tang et al. reported a facile strategy for the synthesis of different *N*-heterocycles such as pyrroles, 2-arylindoles, and quinoxalines. This method consisted of generating a transient amphoteric α-amino aldehyde via Heyns rearrangement. In carbohydrate chemistry, it is known that *in-situ* formed α-amino aldehydes usually undergo intramolecular addition by the hydroxyl group while in this case the key reactive intermediate is successfully captured by inter- or intramolecular carbon and nitrogen nucleophiles (Scheme 5).[10]



Scheme 5. Investigation and application of in situ generated amphoteric α-amino aldehydes based on Heyns rearrangement. Reproduced from ref. [10] Copyright (2016), with permission from American Chemical Society.

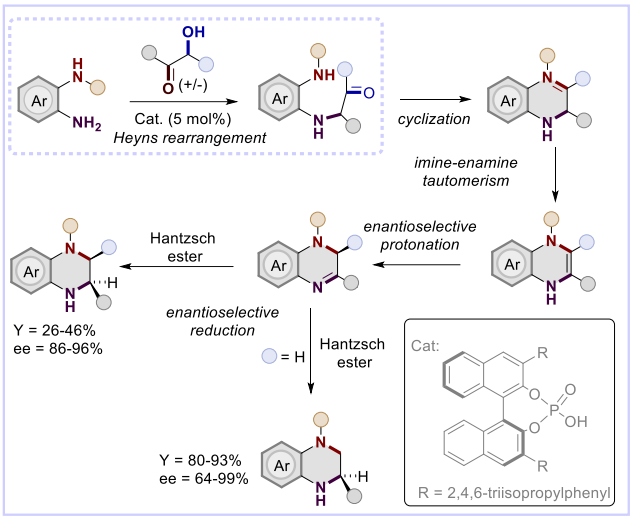
Shortly afterwards, they described the synthesis of complex *N*-heteropolycycles containing tetrahydro-β-carboline in high yield and diastereoselectivity combining for the first time the Heyns rearrangement with a Pictet-Spengler reaction. This Brønsted acid catalyzed tandem reaction proceeded smoothly through the formation of a transient α-amino ketone intermediate, which subsequently undergoes a tandem condensation-Pictet-Spengler reaction (Scheme 6).[11]



Scheme 6. Pictet-Spengler reaction based on in situ generated alpha-amino iminium ions through the Heyns rearrangement. Reproduced from ref. [11] Copyright (2016), with permission from Royal Society of Chemistry.

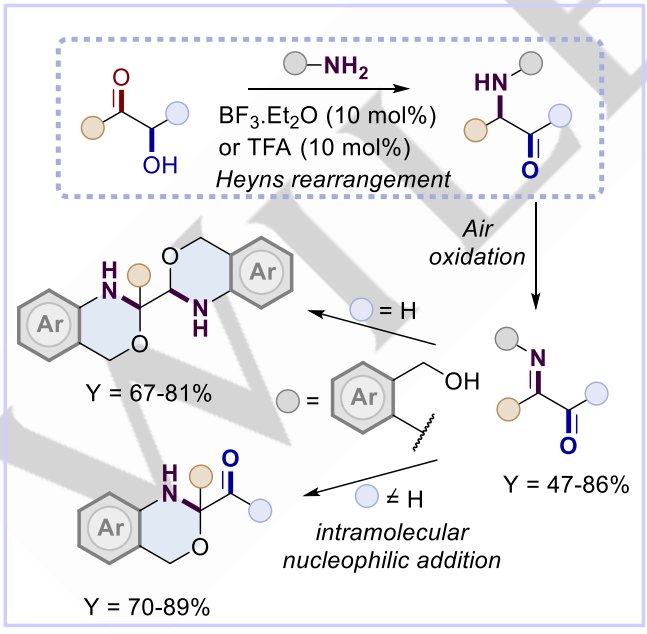
The same research group, in 2021, also synthesized a panel of optically active *N*-substituted tetrahydroquinoxalines by using a simple one-pot catalytic regioselective Heyns rearrangement/enantioselective transfer hydrogenation. The method shows broad substrate scope and excellent functional group tolerance. Diverse α-hydroxyl ketones as well as functionalized o-phenylenediamines reacted effectively to access the corresponding *N*-substituted tetrahydroquinoxaline derivative in good to excellent yields with excellent enantiocontrol (Scheme 7).

The enantioselectivity was rationalized in terms of the model for the mechanism shown in Scheme 7 involving an enantioselective transfer hydrogenation for reactions with primary α-hydroxyl ketones as substrates while racemic secondary α-hydroxyl ketones instead follow a tandem enantioselective protonation-kinetic resolution pathway.[12]



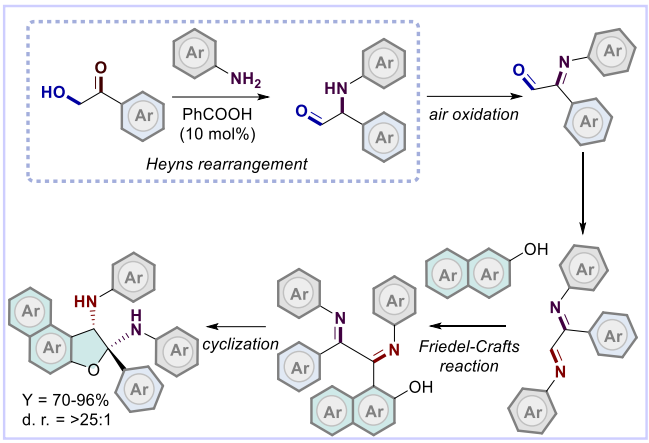
Scheme 7. Investigation and application of in situ generated amphoteric α-amino aldehydes based on Heyns rearrangement. Reproduced from ref. [12] Copyright (2021), with permission from Royal Society of Chemistry.

In 2021, Tang et al. went forward with their research program applying the Heyns rearrangement to the regioselective assembly of α-imino ketones. Their mechanistic studies suggested that the reaction proceeded *via* tandem Heyns rearrangement/oxidation reaction. Interestingly, when extra hydroxyl or amino groups were incorporated in the aromatic amine substrate the reaction effectively proceeded further to access *N, O*-ketals, bicyclic *N, O*-ketals, and 2,3-dihydropyrazines in high yields with good diastereoselectivities. The method shows wide substrate scope and excellent functional group tolerance including primary α-hydroxyl ketones, secondary α-hydroxyl ketones, aromatic and aliphatic amines (Scheme 8).[13]
In continuation of their research, in 2022, Tang and coworkers published also a highly diastereoselective one-pot multicomponent synthesis based on a series of cascade reactions, including Heyns rearrangement, oxidation of amine into imine, Friedel−Crafts reaction, and stereoselective cyclization.



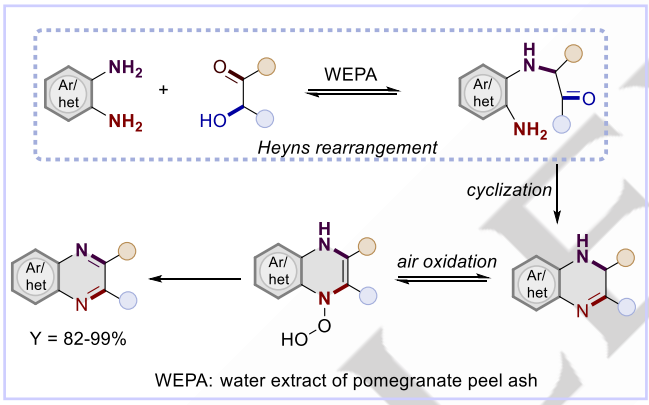
Scheme 8. Preparation and application of α-imino ketones through one-pot tandem reactions based on Heyns rearrangement. Reproduced from ref. [13] Copyright (2021), with permission from American Chemical Society.

This methodology provides a novel green process for the construction of polysubstituted dihydronaphthofurans starting from simple α-hydroxyl ketone, β-naphthols, and aromatic amines (Scheme 9).[14]



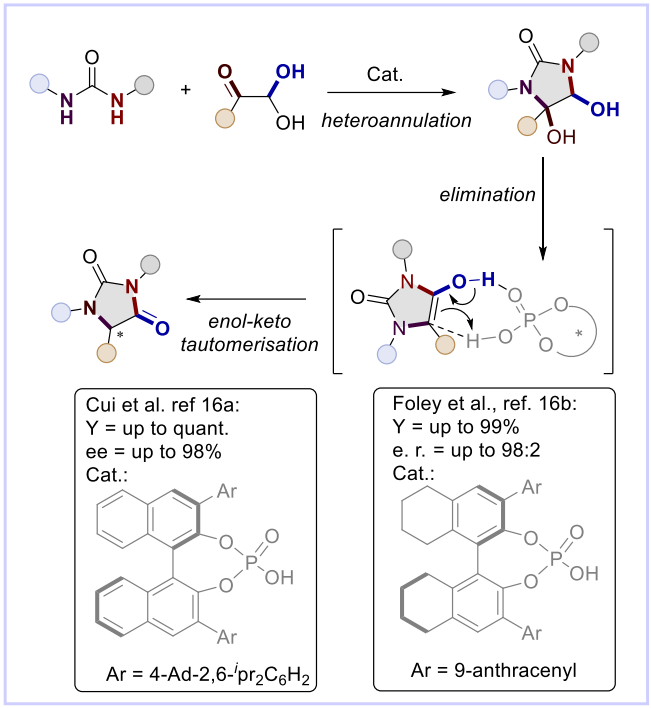
Scheme 9. Preparation of dihydronaphthofurans from α-hydroxyl ketones via a one-pot multicomponent reaction based on Heyns rearrangement. Reproduced from ref. [14] Copyright (2022), with permission from American Chemical Society.

Another appealing green tandem reaction based on Heyns rearrangement was reported by Venkateswarlu et al. in 2022 starting from a variety of aryl/heteroaryl 1,2-diamines and α-hydroxy ketones with aromatic/heteroaromatic/aliphatic substituents *via* a cascade Heyns rearrangement-cyclization-oxidation process in the absence of metal-based catalysts and (or) oxidants. This reaction utilized a waste biomass-derived catalyst (WEPA) and gave access to a variety of functionalized quinoxalines (Scheme 10).[15]



Scheme 10. A reusable waste biomass-derived catalyst for external oxidant/metal-free quinoxaline synthesis via tandem condensation–cyclization–oxidation of α-hydroxy ketones. Reproduced from ref. [15] Copyright (2022), with permission from Royal Society of Chemistry.

An interestingly enantioselective methodology using a chiral phosphoric acid as catalyst and consisting of a tandem [3 + 2] heteroannulation/enantioselective Heyns rearrangement was developed independently by the groups of Foley and Cui in 2023. This methodology allows the obtaining of optically active hydantoins from simple urea and glyoxals in excellent yields and enantioselectivities. The reaction involves the formation of a transient enol intermediate, which is set up for an enantioselective enol-keto tautomerization. The chiral phosphoric acid acts as a proton-transfer to control the enantioselectivity (*via* hydrogen-bonding interactions) during the tautomerization step (Scheme 11).[16]

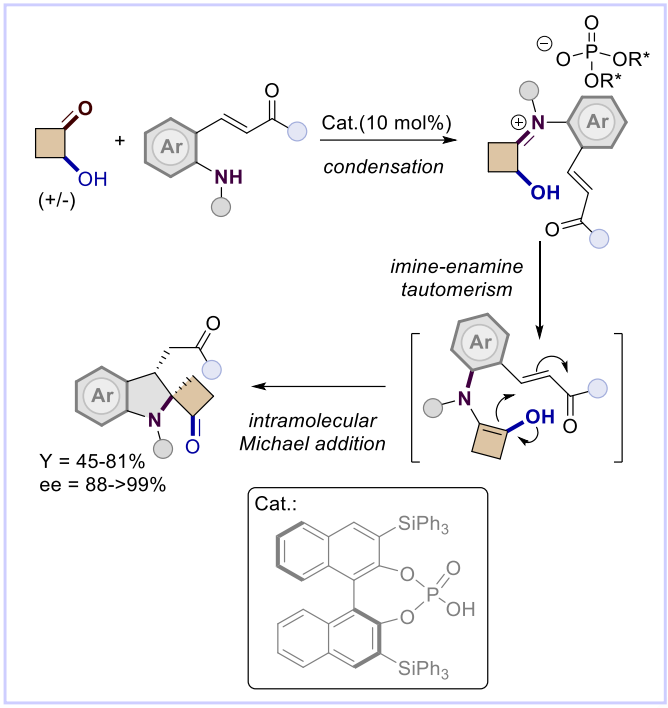


Scheme 11. Enantioselective construction of substituted hydantoins via chiral phosphoric acid catalyzed annulation/Heyns rearrangement of arylsubstituted ureas with glyoxals. Reproduced from ref. [16] Copyright (2023), with permission from Royal Society of Chemistry.

4. Interrupted Heyns Rearrangements

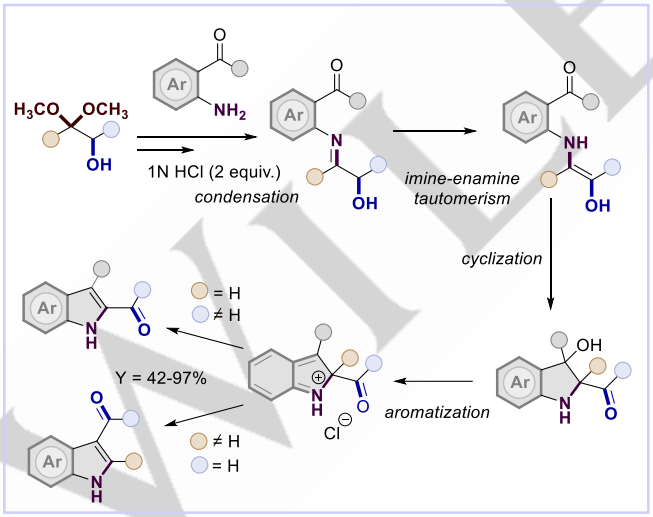
Interrupted rearrangements involve the generation and subsequent trapping of reactive intermediates with a suitable electrophile or nucleophile. This allows for the rapid assembly of complex molecular scaffolds through the formation of new carbon-carbon or carbon-heteroatom bonds. In this regard, in 2023, the Ghorai group made a significant progress in the chemistry of Heyns rearrangement developing for the first time its electrophilic modification by the *in-situ* trapping of the key amino enol intermediate with an α,β-unsaturated carbonyl moiety.

This novel Brønsted acid catalyzed methodology enables the asymmetric synthesis of several valuable spiroindoline and spiropyrrolidine products in good yields with excellent enantio- and diastereoselectivities. Some control experiments carried out by the authors supported the proposed reaction pathway involving a tandem interrupted Heyns rearrangement-intramolecular Michael addition *via* the initial formation of an iminium ion which is subsequently isomerized to the corresponding enamine to yield the corresponding 1-azaspiro cyclobutanone derivative by the formation of a new C−C bond (Scheme 12).[17]



Scheme 12. Access to enantioenriched 1-azaspiro cyclobutanones enabled by modified Heyns rearrangement. Reproduced from ref. [17] Copyright (2023), with permission from Wiley-VCH.

In the same year, Altia and Anbarasan published another interesting example of interrupted Heyns rearrangement. They carried out the regioselective synthesis of 2- and 3-acylindoles, in good to excellent yields, from o-acylanilines and α-hydroxycarbonyls by means of a Brønsted acid catalyzed intramolecular trapping of an *in situ* generated amino enol intermediate with a tethered carbonyl followed by aromatization or rearrangement/aromatization (Scheme 13).[18]

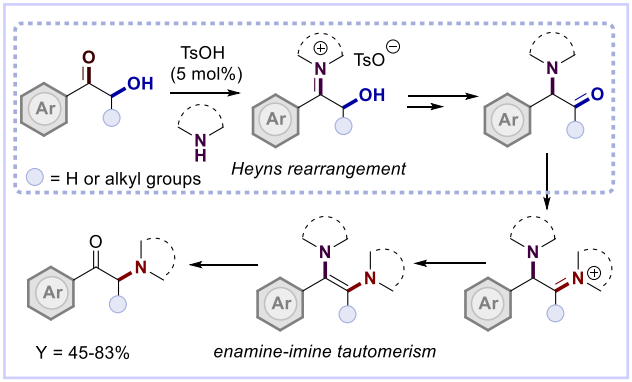


Scheme 13. Interrupted Heyns rearrangement approach for the regioselective synthesis of acylindoles. Reproduced from ref. [18] Copyright (2023), with permission from Royal Society of Chemistry.

5. Consecutive Heyns rearrangements

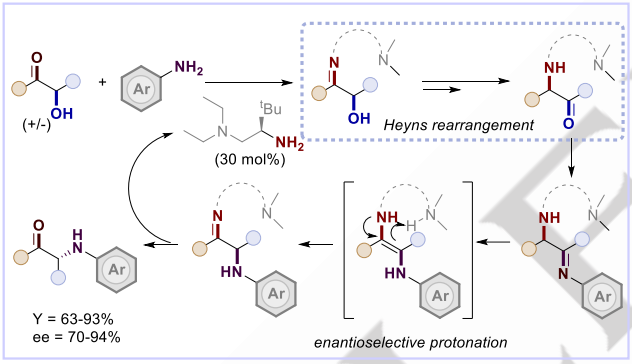
In 2019, Tang et al. developed a tandem reaction sequence based on Heyns rearrangement for the regioselective synthesis of biologically significant α-amino ketones. The reaction was carried out in the presence of catalytic amounts of TsOH using

primary and secondary α-hydroxy aromatic ketones in reaction with aliphatic and aromatic secondary amines, under solvent free conditions. Intriguingly, from a mechanistic point of view the selectivity of the reaction diverged from the traditional Heyns rearrangement. As the authors report in their paper, the reaction process can be seen as the SN-type substitution of the hydroxyl group with an amine group (Scheme 14).[19]



Scheme 14. Synthesis of α-amino ketones from α-hydroxyl ketones via a novel tandem reaction sequence based on Heyns rearrangement. Reproduced from ref. [19] Copyright (2019), with permission from Thieme.

The implications of their discovery are significant as it gains further insights into Heyns rearrangement mechanism and opens avenues for further investigation potentially leading to advancements in organic synthesis.



Scheme 15. Chiral primary amine catalyzed enantioselective tandem reactions based on Heyns rearrangement. Reproduced from ref. [20] Copyright (2022), with permission from American Chemical Society.

In a conceptually related contribution, in 2022, the same research group disclosed an interesting catalytic biomimetic Heyns rearrangement for the synthesis of optically active α-amino ketones. Using simple substrates as starting materials, a broad range of functionalized α-amino ketones were straightforwardly assembled in moderate to good yield and enantioselectivities (up to 94%). The transformation proceeds, in the presence of a chiral primary amine as catalyst, through a tandem condensation- Heyns rearrangement-enantioselective enamine-imine tautomerism without the shift of the carbonyl group (Scheme 15).[20]

6. Summary and Outlook

In conclusion, the Heyns rearrangement, although relatively unknown beyond the area of carbohydrate and food chemistry, offers intriguing opportunities for synthetic chemists to explore new reactions and innovative concepts. Particularly promising is the trend of combining the Heyns rearrangement with other complex reactions and the development of its electrophilic modification (interrupted Heyns rearrangement). Overall, the increasing number of papers published on this topic in recent years reflects the growing credit to the relevance of this topic in organic synthesis. However, despite these significant advances, several challenges persist. One potential limitation of the current Heyns rearrangement lies on its substrate scope. Therefore, additional efforts need to be directed towards the expansion of the reaction scope, for instance encompassing its vinylogous variant and increasing the number of compounds obtainable through tandem reactions based on this rearrangement. Another

important aspect that needs to be addressed is the development of a highly enantioselective catalytic Heyns rearrangement starting from fully aliphatic amines. This outcome would bring Heyns rearrangement to the interest of a greater sphere of researchers opening routes to understanding better the various reactions operative in food chemistry, e.g. the Maillard reaction and related rearrangement. Moreover, new developments in Heyns rearrangement could lead to the discovery of new bioactive compounds and even the development of innovative materials. To conclude, the knowledge discussed in this concept review combined with both experimental and theoretical mechanistic studies, could help researchers to further uncover their synthetic potential and applications. We believe that addressing these challenges will continue to drive advancements in the field of Amadori- and Heyns rearrangements.

7. Acknowledgements

Financial support from the MUR (PNRR 2022, Spoke VS4, WP4.5 Task 4.5.1–RETURN) is acknowledged. C.I.N.M.P.I.S. “Consorzio Interuniversitario Nazionale di Ricerca in Metodologie e Processi Innovativi di Sintesi” is acknowledged.

Keywords: synthetic methods • Heyns rearrangement • α-amino ketones • heterocycles • amines.

[1] (a) M. Amadori, *Atti. R. Accad. Naz. Lincei*, **1925**, *2*, 337. (b) M. Amadori, *Atti. R. Accad. Naz. Lincei*, **1931**, *13*, 72. (c) K. Heyns, W. Z. Koch, *Naturforsch., B*, **1952**, *7*, 486 –488. (d) K. Heyns, H. Noack, *Chem. Ber.* **1962**, *95*, 720–727. (e) T. M. Wrodnigg, B. Eder, Glycoscience-Epimerization Isomerization Rearrangement Reactions of Carbohydrates, A. E. StützSpringer, 2001, pp. 115–152. (f) L. A. Paquette, J. E. Hofferberth, *Org. React.*, **2004**, *62*, 477–567. (g) T. M. Wrodnigg, C. Kartusch, C. Illaszewicz, Carbohydr. Res. **2008**, *343*, 2057–2066. (h) K. Gallas, G. Pototschnig, F. Adanitsch, A. E. Stutz, T. M. Wrodnigg, *Beilstein J. Org. Chem.* **2012**, *8*, 1619–1629. (i) T. M. Wrodnigg, A. E. Stutz, *Angew. Chem. Int. Ed.* **1999**, *38*, 827– 828. (j) K. Maruoka, H. Yamamoto, *Comp. Org. Synth.*, **1991**, *6*, 789 –791.

[2] (a) L. C. Maillard, *C. R. Seances Acad. Sci.*, *Ser. 2*, **1912**, *154*, 66–68. (b) N. Tamanna, N. Mahmood, *Int. J. Food Sci.*, **2015**, *2015*, 526762.

[3] (a) M. N. Lund, C. A. Ray, *J. Agric. Food Chem.* **2017**, *65*, 4537–4552. (b) H. Cui, J. Yu, Y. Zhai, L. Feng, P. Chen, K. Hayat, Y. Xu, X. Zhang, C.-T Ho, *Trends Food Sci. Technol.*, **2021**, *115*, 391–408. (c) A. Adams, N. De Kimpe, *Chem. Rev.* **2006**, *106*, 2299–2319.

[4] (a) R. E. van Outersterp, S. J. Moons, U. F. H., Engelke, H. Bentlage, T. M. A. Peters, A. van Rooij, M. C. D. G. Huigen, S. de Boer, E. van der Heeft, L. A. J. Kluijtmans, C. D. M. van Karnebeek, R. A. Wevers, G. Berden, J. Oomens, T. J. Boltje, K. L. M. Coene, J. Martens, *Commun Biol.* , **2021**, *4*, 367. (b) F. Ledl, E. Schleicher, *Angew. Chem., Int. Ed*. **1990**, *29*, 565−594. (c) N. A. Ansari, D. Dash, *Aging Dis.*, **2013**, *4*, 50–56.

[5] (a) T.M. Wrodnigg, B. Eder, *Top. Curr. Chem.* **2001**, *215*, 115–152. (b) Y. Luo, S. Li, C. Ho, *Molecules*, **2021**, *26*, 4314. (c) V. A. Yaylayan, Huyghues-Despointes, A., *Crit. Rev. Food Sci Nutr*., **1994**, *34*, 321–369. (d) V. A. Yaylayan, *Food Sci. Technol. Res*., **2003**, *9*, 1–6.

[6] A. Frongia, F. Secci, F. Capitta, P. P. Piras, M. L. Sanna, *Chem. Commun.* **2013**, *49*, 8812–8814.

[7] (a) D. J. Aitken, P. Caboni, H. Eijsberg, A. Frongia, R. Guillot, J. Ollivier, P. P. Piras, F. Secci, *Adv. Synth. Catal.* **2014**, *356*, 941−945. (b) N. Melis, L. Ghisu, R. Guillot, P. Caboni, F. Secci, D. J. Aitken, A. Frongia, *Eur. J. Org. Chem.* **2015**, 2015, 4358–4366. (c) A. Frongia, N. Melis, I. Serra, F. Secci, P. P. Piras, P. Caboni, *Asian J. Org. Chem*. **2014**, *3*, 378−381.

[8] J. Cao, Y.-X. Su, X.-Y. Zhang, S.-F. Zhu, *Angew. Chem. Int. Ed.* **2022**, e202212976.

[9] N. Melis, F. Secci, T. Boddaert, D. J. Aitken, A. Frongia, *Chem. Commun.* **2015**, *51*, 15272–15275.

[10] G. X. Li, L. Tang, H. X. Liu, Y. W. Wang, G. Zhao, Z. Tang, *Org. Lett*. **2016**, *18*, 4526−4529.

[11] J. X. Liang, G. B. Yang, Y. P. Zhang, D. D. Guo, J. Z. Zhao, G. X. Li, Z. Tang, *Org. Chem. Front.* **2020**, *7*, 3242−3246.

[12] J. Huang, G. X. Li, G. F. Yang, D. Q. Fu, X. K. Nie, X. Cui, J. Z. Zhao, Z. Tang, *Chem. Sci.* **2021**, *12*, 4789−4793.

[13] L. Li, S. Zhang, X. Deng, G. Li, Z. Tang, G. Zhao *Org. Lett.* **2021**, *23*, 6819–6824.

[14] J. Huang, J.-F. Chen, X. Cui, J.-Z. Zhao, Z. Tang, G.-X. Li, *J. Org. Chem*. **2022**, *87*, 3311–3318.

[15] B. R. Naidu, K. Venkateswarlu, *Green Chem.,* **2022**, *24*, 6215–6223.

[16] (a) Y. Wang, J. Li, Y. Li, C. Pi, Y. Wu, X. Cui, *Org. Chem. Front*., **2023**, *10*, 5631–5636. (b) S. Aryal, C. A. Hone, M. I. J. Polson, D. J. Foley, *Chem. Sci.,* **2023**, *14*, 7905–7912.

[17] S. Pandaand, P. Ghorai, *Angew. Chem.Int. Ed.* **2023**, *62*, e20230617.

[18] M. Altia, P. Anbarasan, *Chem. Commun*., **2023**, *59*, 13747–13750.

[19] L. Y. Li, Q. L. Zeng, G. X. Li, Z. Tang, *Synlett* **2019**, *30*, 694−698.

[20] X.-K. Nie, Y. Chen, S.-Q. Zhang, X. Cui, Z. Tang, G.-X. Li, *Org. Lett.* **2022**, *24*, 2069–2074.