

Organocatalytic Approach in Asymmetric Piancatelli Reactions: An Update

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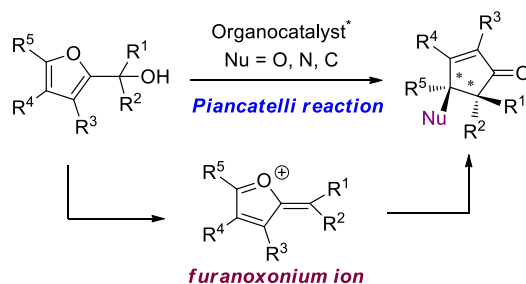
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Abstract- In the Piancatelli reaction, 2-furylcarbinol is converted into functionalized cyclopentenone via an intermediate called furanoxonium and consequent ring opening followed by an electrocyclic reaction of 4 π electron system, was first discovered by Piancatelli in 1976. As a result of this work, important molecular scaffolds have been obtained, which are not only present in a number of natural products, but they are also used to synthesize a variety of bioactive compounds, including prostaglandins, sibirinones, and verrillins naturally found in nature. Several chiral Brønsted acid based on BINOL derived chiral phosphoric acids or pentacarboxycyclopentadiene (PCCP) were utilized for the asymmetric Piancatelli reactions. Here, the complete developments on the asymmetric organocatalytic methods will be discussed till date.

Keywords: Asymmetric organocatalysis, Piancatelli reactions, rearrangement reaction, 2-furylcarbinol.



I. INTRODUCTION

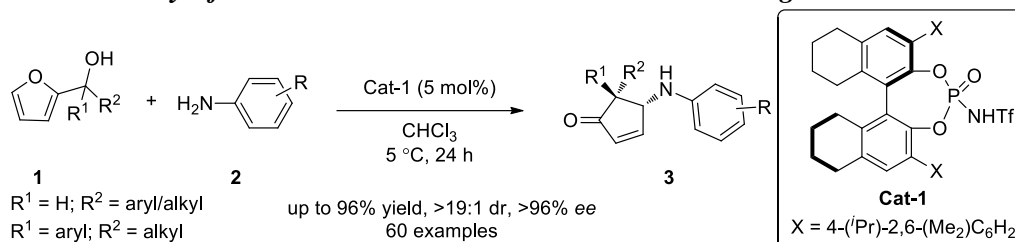
One of the most fundamental methods of promoting and controlling chemical reactions is catalysis.¹ A catalytic process has many benefits, including its efficiency and atom economy, since it uses catalysts in substoichiometric amounts. A variety of industrial processes rely on catalysis, including those in the chemical, pharmaceutical, agrochemical, and polymer industries. In 1909, the Nobel Prize Committee acknowledged the importance of catalysis by awarding Ostwald the Nobel Prize for his pioneering work in catalysis, chemical equilibria, and reaction velocities. Additionally, in the past decade, three Nobel Prizes have been awarded to scientists developing new catalytic concepts (2001 – Knowles, Noyori, Sharpless – catalytic asymmetric hydrogenations and oxidations; 2005 – Chauvin, Grubbs, Schrock – development of new catalysts for metathesis reactions; 2010 – Heck, Negishi, Suzuki – transition metal-catalyzed cross-coupling reactions).

A catalytic process using small organic molecules, known as organocatalysis, has demonstrated great promise as a complementary approach to the transition metal based methods over the past 22 years.²⁻⁵ In asymmetric organocatalysis, small metal-free chiral organic compounds are used as catalysts in this new branch of organic synthesis. During this period, chemical communities studied important but yet basic reactions, creating new tools for generating stereocontrolled chiral compounds. This elite group of chemists David W. C. MacMillan (Princeton University, United States) and Benjamin List (Max-Planck Institut für Kohlenforschung, Germany) were added to in 2021 with the award of the Nobel Prize for the development of asymmetric organocatalysis by the Royal Swedish Academy of Sciences. In modern asymmetric synthesis, enantioselective organocatalysis is recognized as a third pillar following metal complexes and enzymes mediated catalysis.

Piancatelli's reaction, first discovered in 1976, converts 2-furylcarbinol into functionalized cyclopentenone via furanoxonium and a subsequent ring opening followed by an electrocyclic reaction of the 4 π electron system.⁶ A number of important molecular scaffolds have been obtained as a result of this work, which are not only present in natural products but can also be synthesized to produce a variety of bioactive compounds, including prostaglandins,

sibirinones, and verrillins naturally found in nature. In this paper the developments asymmetric Piancatelli reactions using chiral organocatalysts will be discussed.

a. Chiral Brønsted acid catalyst for the enantioselective aza-Piancatelli rearrangement:

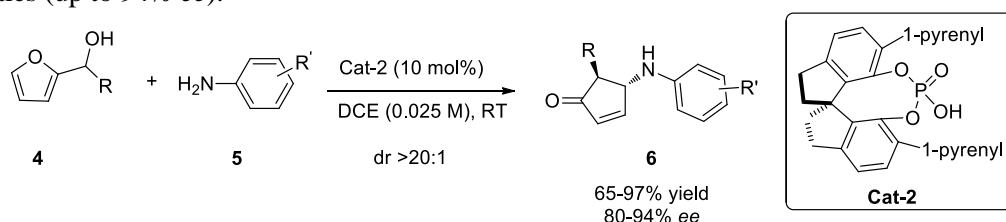


Scheme 1: Chiral Brønsted acid catalyst for the enantioselective aza-Piancatelli rearrangement.

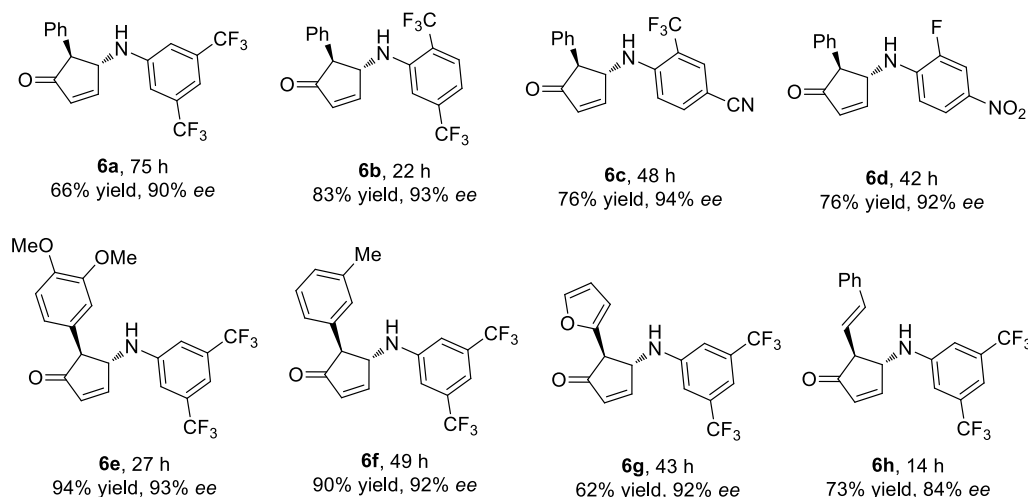
The first organocatalytic enantioselective aza-Piancatelli rearrangement was reported by Rueping and co-workers by the reaction of wide range of 2-furfurylcarbinols **1** with various aniline derivatives **2** using chiral phosphoric acids based Brønsted acid catalyst **Cat-1** in 2016 (Scheme 1).⁷ Numerous aminocyclopentenones **3** were obtained by using 5 mol% catalyst loading with excellent diastereoselection (dr >19:1) and very good yield (up to 96%) and enantioselectivities (up to >96% ee).

b. Chiral Brønsted acid catalyst for the enantioselective aza-Piancatelli rearrangement:

In the same year, Sun and co-workers also reported organocatalytic enantioselective aza-Piancatelli rearrangement by the reaction of readily available 2-furfurylcarbinols **4** with variously substituted anilines **5** using chiral phosphoric acids based Brønsted acid catalyst **Cat-2** (Scheme 2).⁸ Various valuable chiral 4-amino-2-cyclopentenone **6** were obtained by using 10 mol% catalyst loading with excellent diastereoselection (dr >20:1) and very good yield (up to 97%) and enantioselectivities (up to 94% ee).

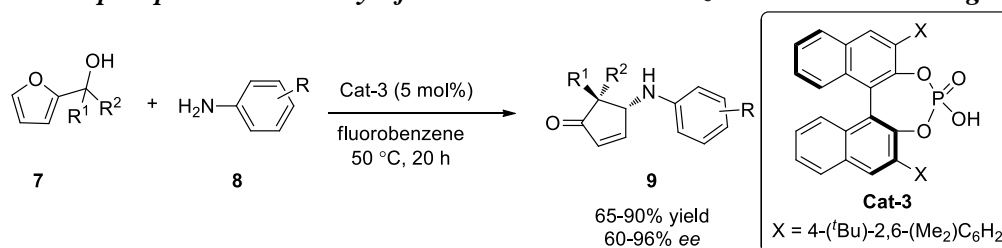


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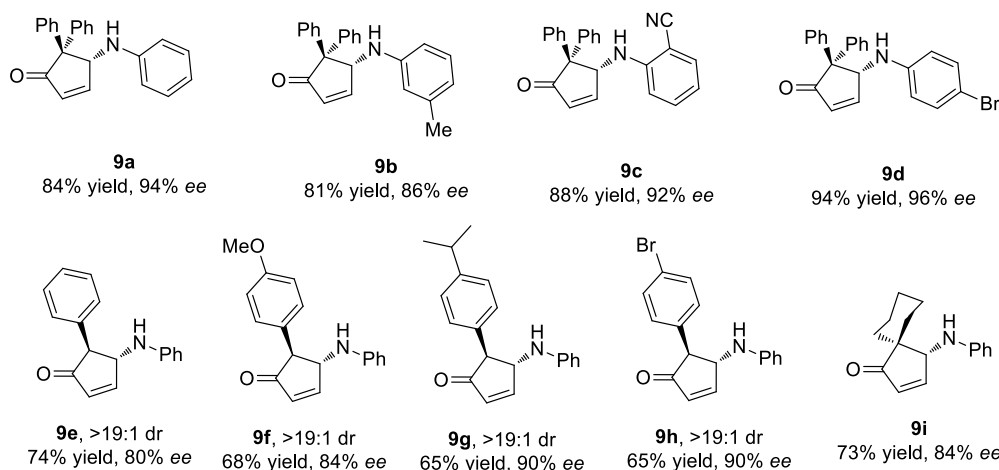


Scheme 2: Chiral Brønsted acid catalyst for the enantioselective aza-Piancatelli rearrangement.

c. Chiral BINOL based phosphoric acid catalyst for the enantioselective aza-Piancatelli rearrangement reaction:



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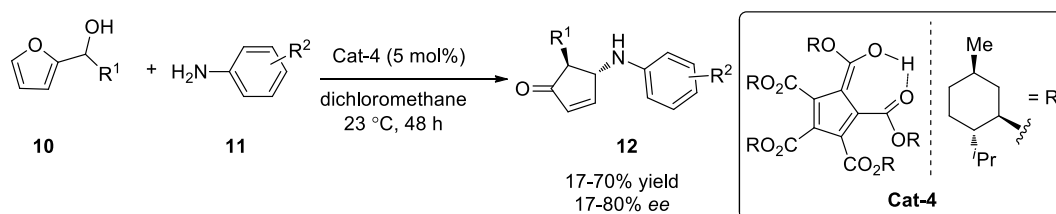


Scheme 3: Chiral phosphoric acid catalyst for the enantioselective aza-Piancatelli rearrangement.

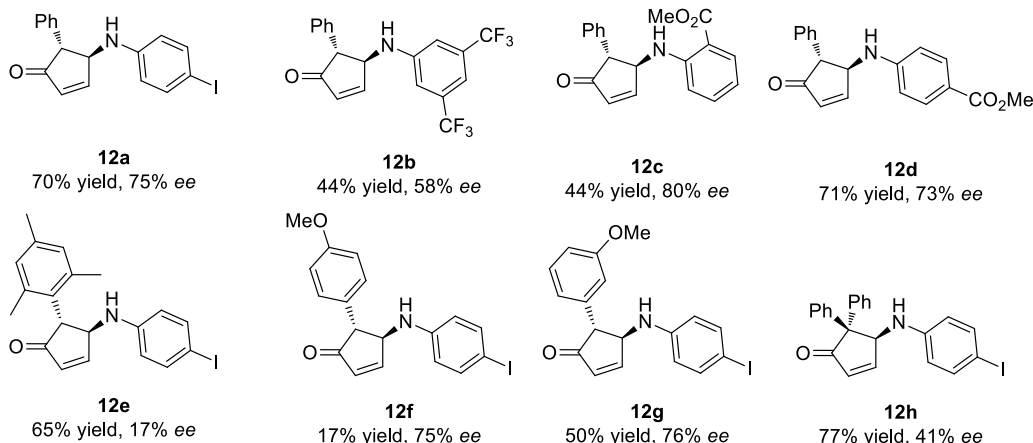
In further report towards the development of enantioselective aza-Piancatelli rearrangement reaction, Pati and co-workers reported the stereoselective reaction between furylcarbinols **7** with various anilines **8** using the chiral phosphoric acid catalyst **Cat-3** (Scheme 3).⁹ A varieties of highly functionalized cyclopentenones **9** were obtained with high yields and excellent diastereo and enantioselectivities (up to 97% yield, >19:1 dr, 94% ee) when the reaction was conducted in presence of 5 mol% catalyst loading at 50 °C for 20 h.

d. Chiral BINOL based phosphoric acid catalyst for the enantioselective aza-Piancatelli rearrangement reaction:

Towards the development of an alternative to chiral phosphoric acid based catalyst, in 2019, Alaniz and co-workers developed pentacarboxycyclopentadiene (PCCP) based chiral Brønsted acid catalyst **Cat-4** for the enantioselective aza-Piancatelli rearrangement (Scheme 4).¹⁰ In order to control the aza-Piancatelli's stereochemistry, an inexpensive and readily available chiral Brnsted acid PCCP catalyst could be used. The chiral PCCP catalyzed aza-Piancatelli rearrangement reaction shows good substrate scope and is successful with a range of aniline **11** and furylcarbinol derivatives **10** to obtain the desired products **12** with up to 70% isolated yield and 80% enantioselectivities.



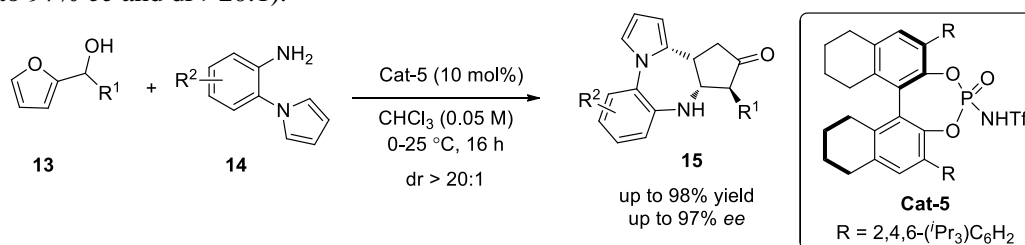
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Scheme 4: Chiral pentacarboxycyclopentadiene catalyst for the enantioselective aza-piancatelli rearrangement.

e. Chiral Brønsted acid catalyst for the enantioselective aza-piancatelli rearrangement/Friedel–Crafts alkylation cascade reaction:

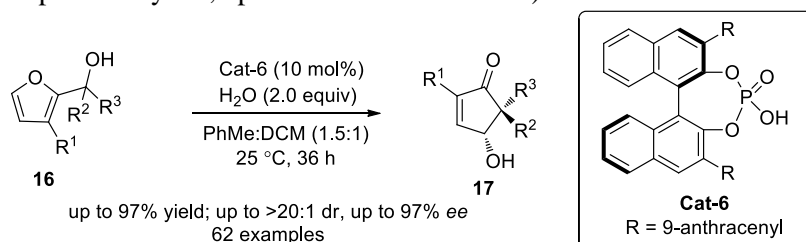
In the same year, Jiang and co-workers developed a new method for the enantioselective aza-piancatelli rearrangement/Friedel–Crafts alkylation cascade reaction using chiral Brønsted acid catalyst **Cat-5** (Scheme 5).¹¹ Enantioenriched cyclopenta[*f*]pyrrolo[1,2-*d*][1,4]diazepinones bearing three contiguous stereocenters **15** were obtained from a wide range of both readily available 2-furylcarbinols **13** and (1*H*-pyrrol-1-yl)anilines **14** by using 10 mol% catalyst **Cat-5** with good to excellent yields as well as chemo-, enantio-, and diastereoselectivities (up to up to 98% yield, up to 97% ee and dr >20:1).



Scheme 5: Chiral Brønsted acid catalyst **Cat-5** for the enantioselective aza-piancatelli rearrangement/Friedel–Crafts alkylation cascade reaction.

c. Chiral BINOL derived phosphoric acid for the enantioselective oxa-piancatelli rearrangement reaction:

Recently, Schneider and co-workers developed chiral BINOL derived phosphoric acid **Cat-6** catalyzed enantioselective oxa-piancatelli rearrangement reaction (Scheme 6).¹² A wide range of furfurylcarbinols **16** were converted to densely substituted γ -hydroxy cyclopentenones **17** by using 10 mol% catalyst **Cat-6** with excellent diastereo- and enantioselectivities (up to up to 97% yield, up to 97% ee and dr >20:1).



Scheme 6: Chiral BINOL derived phosphoric acid **Cat-6** for the enantioselective oxa-piancatelli rearrangement reaction.

II. CONCLUSION

In this paper we thoroughly reviewed the complete developments of the Organocatalytic enantioselective processes.

III. ACKNOWLEDGMENT

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REFERENCES:

1. G. Ertl, H. Knözinger, J. Weitkamp, Eds. Handbook of Heterogeneous Catalysis; Wiley-VCH: New York, **1997**.
2. S. Mukherjee, J. Woon Yang, S. Hoffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471.
3. S. H. Xiang, B. Tan, *Nat Commun.* 2020, *11*, 3786.
4. B. Han, X.-H. He, Y.-Q. Liu, G. He, C. Peng, J.-L. Li, *Chem. Soc. Rev.*, **2021**, *50*, 1522.
5. O. García Mancheño, M. Waser, *Eur. J. Org. Chem.*, **2023**, *26*, e202200950.
6. G. Piancatelli, A. Scettri, S. Barbadoro, *Tetrahedron Lett.* **1976**, *17*, 3555.
7. Y. F. Cai, Y. R. Tang, I. Atodiresei, M. Rueping, *Angew. Chem. Int. Ed.* **2016**, *55*, 14126.
8. H. Li, R. Tong, J. Sun, *Angew. Chem. Int. Ed.* **2016**, *55*, 15125.
9. A. B. Gade, N. T. Patil, *Synlett* **2017**, *28*, 1096.
10. G. R. Hammersley, M. F. Nichol, H. C Steffens, J. M. Delgado, G. K. Veits, J. Read de Alaniz, *Beilstein J. Org. Chem.* **2019**, *15*, 1569.
11. Z. Wei, J. Zhang, H. Yang, G. Jiang, *Org. Lett.* **2019**, *21*, 2790.
12. R. Sarkar, A. Korell, C. Schneider, *Chem. Commun.* **2024**, *60*, 3063.