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# Access to saturated *aza*-heterocycles using the Borrowing Hydrogen methodology

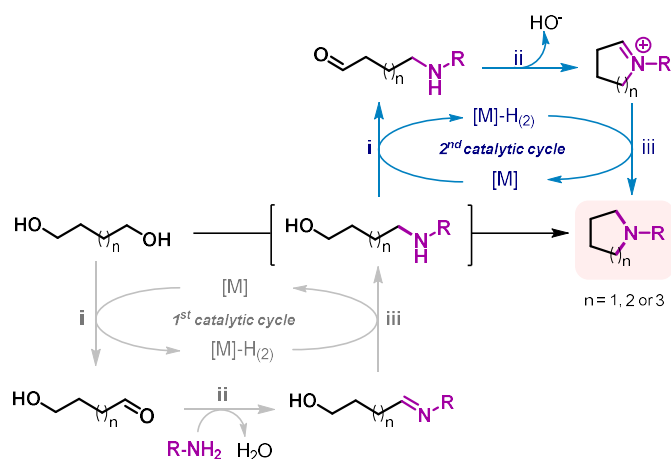
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**Abstract:** Borrowing hydrogen (BH) has reached a wide attention from the chemistry community as a new opportunity to construct efficiently C-N bond (as well as C-C or C-S bond) without any activation. This straightforward strategy is usually supported by relevant organometallic catalysts, involved in the dehydrogenation-reduction processes. This short review highlights specifically the application of the borrowing hydrogen to the preparation of saturated aza-heterocycles (piperidines, pyrrolidines and piperazines) extensively present in high-added value molecules of pharmaceutical industry, with focus on appropriate metals (noble metals and more recently non noble metals) used for this transformation. An extension to chiral induction in order to prepare enantiopure *N*-heterocycles will be also reported.

## Introduction

The concept of borrowing hydrogen (BH) is a very powerful tool for the direct construction of C-N bonds, using alcohols and amines, avoiding the use of highly toxic reagents and the generation of a large amount of waste.<sup>1</sup> The general BH approach relies on a three-step sequence: **i.** organometallic catalyst (Ru, Ir, Fe, Ni and so on) catalyzed oxidation of an alcohol to the corresponding carbonyl compound, **ii.** condensation of the aldehyde/ketone with an amine to generate an imine/enamine with elimination of water as sole by-product, and **iii.** reduction of the imine by the hydrogen stored by the metal catalyst (Scheme 1 – 1<sup>st</sup> catalytic cycle). Over the last few decades, a great enthusiasm has been devoted to explore this methodology for the synthesis of saturated aza-heterocycles, which are present in a large class of biologically molecules and natural products.<sup>2</sup> Up to now, the preparation of cyclic amines has often relied on multi-step reactions,<sup>3</sup> making this BH strategy particularly attractive. In this case, the reaction of an amine (ammonia or primary amine) with a diol proceeds through a repeated BH reaction as shown on Scheme 1 (1<sup>st</sup> and 2<sup>nd</sup> catalytic cycle) leading to pyrrolidine, piperidine or azepane depending on the alkyl chain length of the diol. After a focus on appropriate metals used for this transformation (mainly ruthenium, iridium plus others), an extension to the stereoselective induction in order to prepare enantiopure saturated aza heterocycles will be discussed.

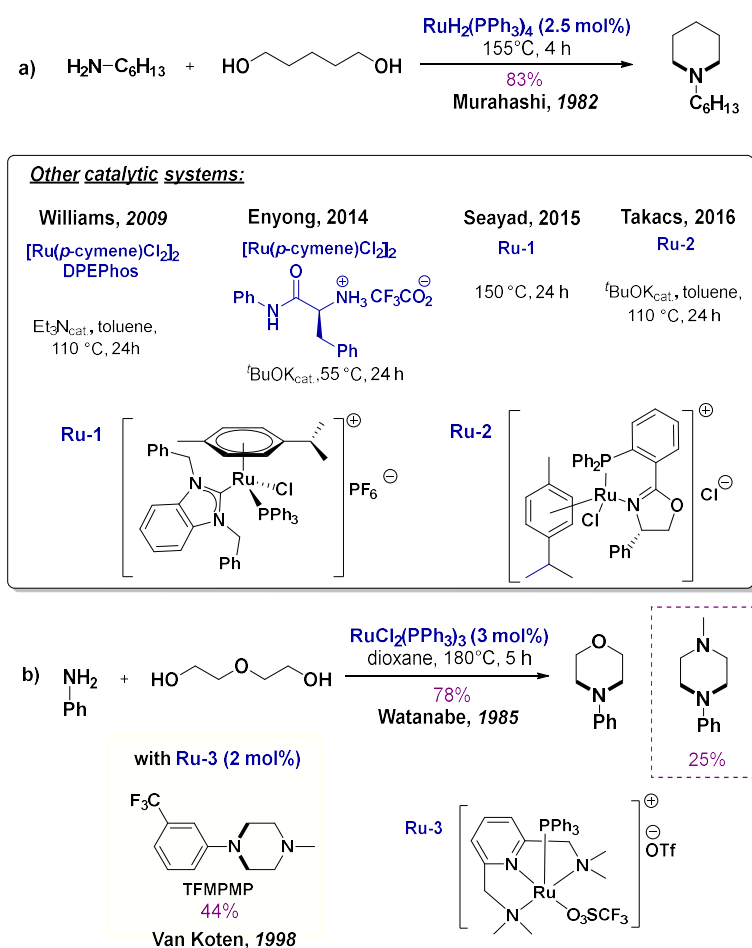


**Scheme 1.** General mechanism for the synthesis of saturated aza-heterocycles using the BH approach

To the exception of Grigg who reported the synthesis of 1-benzylpyrrolidine from benzylamine and an excess of 1,4-butanediol (10 eq.) in the presence of rhodium catalyst  $[\text{Rh}(\text{PPh}_3)_4]$ ,<sup>4</sup> the most widely used noble metals for this transformation remain ruthenium and iridium.

## Ruthenium Catalysis

Seminal work, reported by Murahashi in 1982, described the preparation of 1-hexylpiperidine from a stoichiometric quantity of 1,5-pentanediol and hexylamine in the presence of 2.5 mol% of  $\text{RuH}_2(\text{PPh}_3)_4$  at 155°C during 4 hours in 83% yield (Scheme 2a).<sup>5</sup> A few years later in 2009, Williams reported the *N*-heterocyclization of amines with diols using 2.5 mol% of  $[\text{Ru}(\textit{p}\text{-cymene})\text{Cl}_2]_2$ , 5 mol% of bis-[2-(diphenylphosphino)phenyl]ether ligand (DPEPhos) and 10 mol% of  $\text{Et}_3\text{N}$  in refluxing toluene within 24 hours producing an extended family 5 to 7-aza-membered rings in 33-87% yield.<sup>6</sup> Microwave activation under solvent-free conditions, instead of thermic activation allowed an improvement of the yield with the same combination of ruthenium precursor and ligand.<sup>7</sup> Replacement of DPEPhos ligand by phenylalanine derived ligand (6 mol%) in combination with 3 mol% of  $[\text{Ru}(\textit{p}\text{-cymene})\text{Cl}_2]_2$  was reported by Enyong in quantitative yield at remarkably low temperature (55°C) (Scheme 2a).<sup>8</sup> Many contributors have reported their efforts in different catalytic systems to access pyrrolidines, piperidines or azepanes such as Seayad who prepared air and moisture stable ruthenium *N*-heterocyclic carbene **Ru-1** that was successfully evaluated as a unique catalyst,<sup>9</sup> or Takacs who developed a phosphinoxazoline ruthenium complex **Ru-2**.<sup>10</sup>



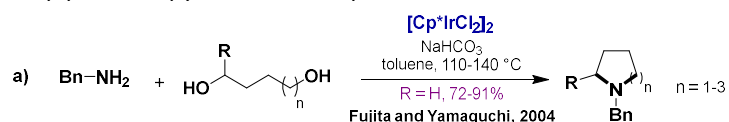
**Scheme 2.** [Ru]-catalyzed annulation of diols and diethyleneglycol

Recently, Xu and co. extended the reaction to 1,2,4-butanetriol, affording in the same mechanism 3-hydroxy-pyrrolidines, by using a combination of  $[\text{Ru}(\textit{p}\text{-cymene})\text{Cl}_2]_2$  (5 mol%), Xantphos (10 mol%) with a scope with only anilines diversely substituted, demonstrating chemoselective control during the borrowing hydrogen procedure.<sup>11</sup> Watanabe changed the catalytic system and adapted smoothly the conditions (using  $\text{RuCl}_2(\text{PPh}_3)_3$  in 3 mol% with a 50% excess of diol). Starting from diethyleneglycol or *N*-substituted diethanolamine, the reaction was extended respectively to the preparation of substituted

morpholine and piperazine in 5 hours. The reactions required harsh conditions of temperature, leading to a moderate yield of 25% when *N*-methyldiethanolamine was used as a substrate for the preparation of 1-methyl-4-phenylpiperazine (Scheme 2b).<sup>12</sup> The ruthenium catalysis was applied successfully to the preparation of some molecules of interest such as TFMPMP, a potent serotonin agonist. The NN'-N-containing ruthenium(II) catalyst **Ru-3** was more active than RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> with a load of 2 mol% at 180°C leading to TFMPMP in 44% yield (Scheme 2b).<sup>13</sup>

## Iridium Catalysis

In 2004, Fujita and Yamaguchi reported the *N*-heterocyclization of benzylamine with diols in toluene at 110°C for 17 hours using 1-2 mol% of [Cp\*IrCl<sub>2</sub>]<sub>2</sub> giving the five-, six-, and seven-membered cyclic amine in 72 to 91% yield (**Erreur ! Source du renvoi introuvable.a**). Noticeably, addition of a base such as NaHCO<sub>3</sub> was required to activate the iridium(III) catalyst and to enhance the reaction. Although the scope of the reaction was wide, when anilines were used as reagents, higher catalytic loadings (5 mol%) and higher temperatures (130 °C) were required.<sup>14</sup> Later, the same methodology was applied for the double *N*-cycloalkylation of *p*-xylenediamine with 1,4-butanediol affording the 1,4-bis(pyrrolidin-1-ylmethyl)-benzene in 95% yield.<sup>15</sup> Interestingly, ammonium salts, which are easily and safely handled compared to ammonia, could also undergo BH amination with diols. The reaction of 1-phenyl-1,5-pentanediol and 1-phenyl-1,4-butanediol with ammonium tetrafluoroborate in the presence of [Cp\*IrCl<sub>2</sub>]<sub>2</sub> and NaHCO<sub>3</sub> at 140°C without any solvent gave the corresponding piperidines and pyrrolidines with 85 and 62 % yield respectively (Scheme 3a).<sup>16</sup> Madsen *et al.* also applied those reaction conditions either in toluene or in water for the synthesis of piperazines using 1,2-diamines and 1,2-diols.<sup>17</sup> Dong and Zhao later demonstrated that the use of microwave irradiation could be beneficial for the reaction. Indeed, the synthesis of saturated aza-heterocycles was reported using 1 mol% of [Cp\*IrCl<sub>2</sub>]<sub>2</sub> without any base or solvent under microwave irradiation at 140 °C for 1 hour. Noticeably, for 5 and 7-membered *N*-heterocycles, a higher reaction temperature of 160 °C was required to reach complete conversion.<sup>18</sup> Trudell also reported the use of microwave irradiation for the synthesis of nicotine and anabasine derivatives using the BH strategy. Reaction time could be reduced from 17 hours using thermal activation to 2 hours using microwave irradiation.<sup>19</sup> Williams also showed that the reaction of  $\alpha$ -methylbenzylamine with a diol could be performed in water at 115 °C without requiring any base using the SCRAM catalyst [Cp\*Ir]<sub>2</sub> (Scheme 3a). Under those reaction conditions, the corresponding pyrrolidine, piperidine, pyrazine and azepane were obtained within 56 to 95% yields.<sup>20</sup>



### Other conditions with [Cp\*IrCl<sub>2</sub>]<sub>2</sub>

- Fujita and Yamaguchi, 2008 : with NH<sub>4</sub>BF<sub>4</sub> as ammonium source (R = Ph, 62-85%)
- Dong and Zhao, 2011 : neat, MW, 140-160°C, 1 h (R = H, 53-81%)
- Trudell, 2013 : Na<sub>2</sub>CO<sub>3</sub>, water, MW, 110 °C, 2 h (R = pyridinyl, 75%)

### Other catalytic systems

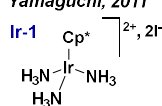
Williams, 2010



water  
115 °C, 15 h

with  $\alpha$ -methylbenzylamine  
(56-95%)

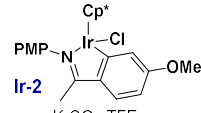
Fujita and Yamaguchi, 2011



water, reflux, 24 h

with benzylamine  
(74-94%)

Wang and Xiao, 2015



K<sub>2</sub>CO<sub>3</sub>, TFE,  
100 °C, 24 h

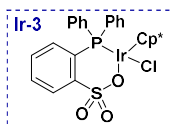
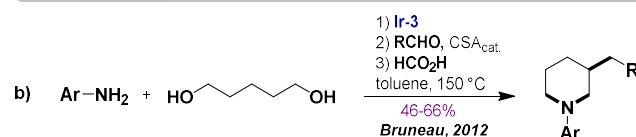
with anilines  
(43-99%)

Williams, 2005



3Å MS, toluene,  
reflux, 24 h

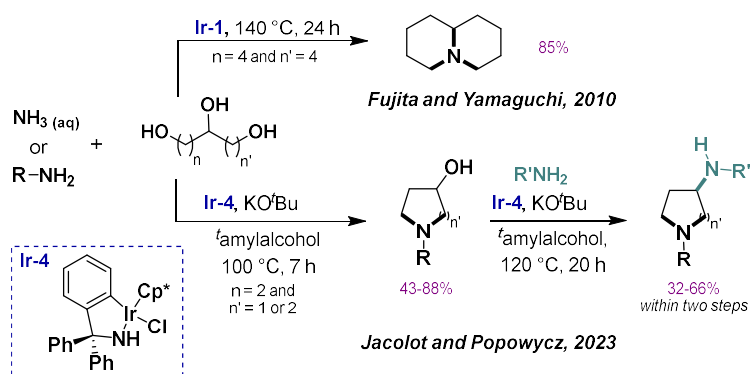
with tryptamine  
(40-83%)



Scheme 3. [Ir]-catalyzed annulation of diols

In 2012, Bruneau *et al.* also took advantage of the BH methodology to develop the tandem *N*-heterocyclization / alkylation reaction using **Ir-3**, an iridium complex bearing a phosphinesulfonate ligand (**Erreur ! Source du renvoi introuvable.b**). The reaction proceeds as follow: anilines first reacted with 1,5-pentanediol in the presence of **Ir-3** (3 mol%), then benzaldehyde derivatives were added and trapped by the endocyclic enamine intermediate. The final reduction step assisted by formic acid, an external reducing agent, led to C-3 alkylated piperidines within 46 to 66% yields.<sup>21</sup>

Similarly, triols could be subjected to BH annulation with amines. Fujita and Yamaguchi reported the synthesis of quinolizidine in 85% yield from 1,5,9-nonanetriol and aqueous ammonia in the presence of the water soluble **Ir-1** catalyst at 140 °C for 24 hours (Scheme 4). In this transformation, the *N*-alkylation proceeds thrice leading to quinolizidine in 85% yield.<sup>22</sup> In 2023, Jacolot and Popowycz reported the synthesis of 3-pyrrolidinols and 4-piperidinols combining triols with primary amines in *t*-amyl alcohol using iridacycle **Ir-4** as catalyst. Noticeably, better results were obtained when a catalytic amount of <sup>t</sup>BuOK, was added to activate the catalyst. Taking advantage of the third hydroxyl group, the methodology was further extended to the sequential diamination of triols affording 3-aminopyrrolidines and 4-aminopiperidines (**Erreur ! Source du renvoi introuvable.**).<sup>23</sup>

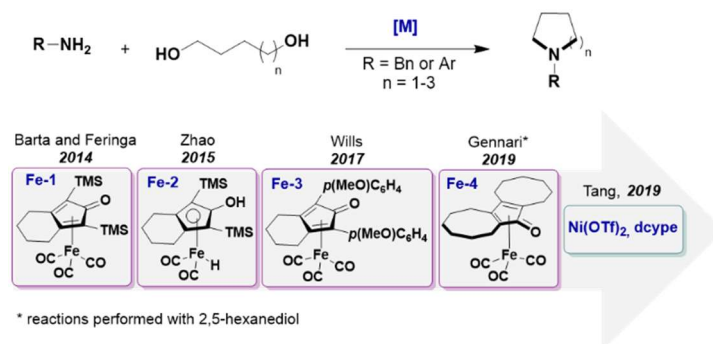


**Scheme 4.** [Ir]-catalyzed annulation of triols

## Other metals

Confronted with the hegemony of iridium and ruthenium, widely used in the BH transformation, alternatives for less-noble metals have emerged in the recent years to overcome the economic cost and improve the sustainable character of this transformation such as iron and to a less extent nickel (Scheme 5).

In 2014, Feringa and Barta reported the synthesis of 5-, 6- and 7-membered rings catalyzed by Knölker's modified catalyst **Fe-1** (5 mol%) activated by trimethylamine *N*-oxide (10 mol%) at 120-130°C in CPME, providing a family of 6 derivatives with a range of yields varying from 60% to 85%.<sup>24</sup> Although the most common synthetic strategy for the preparation of saturated aza-heterocycles is the annulation of diols in the presence of a primary amine, versatile synthetic routes were investigated. As an example, *N*-benzylpiperidine could be synthesized either from benzylamine and 1,5-pentanediol or from benzyl alcohol and 5-aminopentan-1-ol under the same experimental conditions.<sup>25</sup> During the same period, Zhao promoted the direct use of Knölker's catalyst **Fe-2** (10 mol%) at 110°C in toluene during 24 hours using AgF (40 mol%) as additive.<sup>26</sup> Only one example of intramolecular borrowing hydrogen was reported with this set of conditions (condensation of 1,5-butanediol with *p*-anisidine in 61% yield). In 2017, Wills reported a modification of the Feringa catalyst **Fe-1** that allowed the reaction of aniline on hexane-1,6-diol with a moderate yield of 43% with 10 mol% of loading (and activation with Me<sub>3</sub>NO at 9 mol%).<sup>27</sup> Noticeably a better yield (87%) was observed with 3-trifluorobenzylamine. The work of Gennari, with modification using larger cyclooctane on the cyclopentadienone part (**Fe-4**) allowed the amination of primary amines and anilines on more hindered 2,5-hexanediols affording 2,5-dimethylpyrrolidines in 43 to 71% yields after 72 hours.<sup>28</sup> All the iron catalysts used for the transformation by well-known groups share in common a fine tuning around the Knölker's complex.

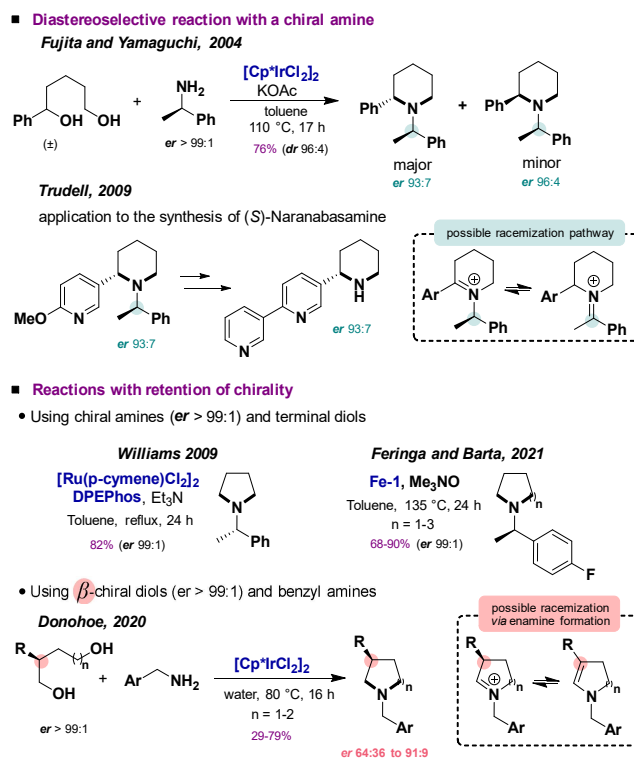


**Scheme 5.** Emergence of other catalysts (iron and nickel)

In 2019, Tang reported the annulation of 1,5-pentanediol with aniline in 89% yield by using 3 mol% of Ni(OTf)<sub>2</sub> and 3 mol% of 1,2-bis(dicyclohexylphosphino)-ethane (dcype), in HFIP solvent (Scheme 5).<sup>29</sup> The conditions could be extended to a wide range of saturated *N*-heterocycles, such as pyrrolidines, piperidines, azepanes and tetrahydroquinoxaline when 1,2-phenylenediamine and 2,3-butanediol were used.

## Stereoselective induction

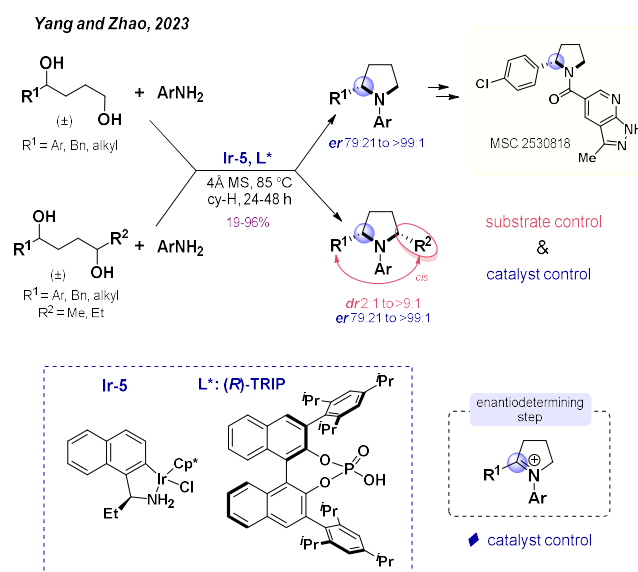
Despite their importance as biologically active compounds<sup>2</sup> or in the field of asymmetric aminocatalysis,<sup>30</sup> the preparation of chiral saturated *N*-heterocycles still often involves multi-step reaction sequences.<sup>31</sup> In the light of this observation, in 2004, Fujita and Yamaguchi applied the BH annulation for the asymmetric synthesis of 2-substituted piperidine using the chiral (*R*)-1-phenylethylamine and 1-phenyl-1,5-pentanediol (**Erreur ! Source du renvoi introuvable.**). The reaction was carried out using [Cp\*IrCl<sub>2</sub>]<sub>2</sub> and KOAc as a base in toluene at 100 °C for 17 hours and led to the corresponding 2-substituted piperidine in 76% yield and with 96:4 dr.<sup>14</sup> This strategy was further applied to the synthesis of both enantiomers of Naranabasamine by Trudell and co-workers.<sup>32</sup> In both cases, despite the use of  $\alpha$ -methylbenzylamine enantiomerically pure (er > 99:1), a slight racemization (93:7 < er < 96:4) was observed, probably due to isomerization of the iminium intermediate shown in Scheme 6.



**Scheme 6.** Diastereoselective reactions with chiral substrates

The non-trivial retention of stereochemistry of either chiral amines or chiral diols in BH cascade reactions were later investigated (Scheme 6). In 2009, Williams *et al.* reported the synthesis of (*S*)-1-(1-phenylethyl)pyrrolidine by *N*-heterocyclization of (*R*)-1-phenylethylamine with 1,4-butanediol using [Ru(*p*-cymene)Cl<sub>2</sub>]<sub>2</sub>, DPEPhos and Et<sub>3</sub>N, without any loss of stereochemical integrity.<sup>6</sup> In 2021, Feringa and Barta also reported a complete retention of chirality for the *N*-alkylation (*R*)-*p*-fluorophenylethylethylamine with terminal diols using **Fe-1** and Me<sub>3</sub>NO in toluene at 135 °C for 24 hours.<sup>33</sup> In 2020, Donohoe *et al.* disclosed an iridium-catalyzed annulation strategy for the asymmetric synthesis of C-3 substituted saturated aza-heterocycles using  $\beta$ -chiral diols and benzylamines (Scheme 6). A wide range of C-3 substituted pyrrolidines and piperidines were thus synthesized with 64:36 to 93:7 er. The partial racemization is likely to occur *via* the enamine formation and could be minimized using water as solvent. Noticeably, lower levels of enantio-retention were observed with bulkier (naphthyl,  $\alpha$ -methylphenyl) and electron-enriched (*p*-OMe, 3,4-methylenedioxy) benzylamines.<sup>34</sup>

In 2023, Yang and Zhao achieved a major breakthrough for the synthesis of chiral saturated *N*-heterocycles. They reported the first enantio-convergent aminative annulation of racemic diols with anilines using the borrowing hydrogen catalysis (Scheme 7).<sup>35</sup> Their success relies on a cooperative catalysis between a chiral iridacycle **Ir-5** and a chiral phosphoric acid (*R*)-TRIP. On contrary to their previous work on enantioselective amination,<sup>36</sup> the configuration of the chiral pyrrolidine is controlled by the chirality of the iridium complex instead of the phosphoric acid. A wide range of 2-substituted pyrrolidines was obtained from 1-substituted-1,4-butanediols and anilines using 2.5 mol% of **Ir-5**, 2.5 mol% of (*R*)-TRIP in the presence of 4Å MS in cyclohexane at 85 °C for 24 to 48 hours in good yields and enantioselectivities. Although broad, the scope of the reaction remained limited to anilines or *N*-heterocyclic amines. The use of benzylamine led to the formation of the cyclization product in 75% yield, but with a modest ratio of 69:31. Notably, this strategy allowed the direct preparation of a key precursor of MSC 2530818, a potent CDK8 inhibitor (Scheme 7).<sup>37</sup>



The more challenging access to chiral di-substituted pyrrolidines was also investigated using the previously depicted reaction conditions. Pyrrolidines were obtained as a mixture of diastereoisomers in ratio 2:1 to > 9:1 depending of the nature of the 1,4-disubstituted-1,4-butanediols. This transformation involves two stereoselective steps: the substrate first controls the diastereoselectivity of the reaction (rather in favor of the *cis*) while the enantioselectivity-determining step is controlled by the catalyst, resulting in match/mismatch effects depending on the substituents.

## Conclusion

The saturated nitrogen-heterocycles are widely present in the pharmaceutical industry: regarding the top 100 most frequently used ring systems from small molecule drugs listed by FDA, piperidine and pyrrolidine rank respectively the 3<sup>rd</sup> and 8<sup>th</sup> position.<sup>38</sup> The borrowing hydrogen amination reaction was first developed in an intermolecular fashion before being extended to intramolecular versions, with diastereoselective and/or enantioselective controls.<sup>39</sup> Interestingly, this BH

reaction can also be coupled to other intramolecular reactions to access novel scaffolds of interest such as the Pictet Spengler reaction or other BH cascade reactions (tetrahydro- $\beta$ -carbolines,<sup>29,40</sup> tetrahydroquinolines,<sup>41</sup> tetrahydropyridines,<sup>42</sup> etc.). Even if iridium and ruthenium remain the most currently used metals involved in this transformation, recent developments with less-noble metals should open opportunities for larger applications.

## References

- [1] For recent reviews, see: a) A. Corma, J. Navas, M. J. Sabater, *Chem. Rev.* **2018**, *118*, 1410–1459. b) B. G. Reed-Berendt, K. Polidano, L. C. Morrill, *Org. Biomol. Chem.* **2019**, *17*, 1595–1607. c) B. G. Reed-Berendt, D. E. Latham, M. B. Dambatta, L. C. Morrill, *ACS Cent. Sci.* **2021**, *7*, 570–585. d) E. Podyacheva, O. I. Afanasyev, D. V. Vasilyev, D. Chusov, *ACS Catal.* **2022**, *12*, 7142–7198. e) S. Hameury, H. Bensalem, K. De Oliveira Vigier, *Catalysts* **2022**, *12*, 1306.
- [2] E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.* **2014**, *57*, 10257–10274
- [3] C.-V. T. Vo, J. W. Bode, *J. Org. Chem.* **2014**, *79*, 2809–2815.
- [4] R. Grigg, T. R. B. Mitchell, S. Sutthivaiyakit, N. Tongpenyai, *J. Chem. Soc., Chem. Commun.* **1981**, 611–612.
- [5] S.-H. Murahashi, K. Kondo, T. Hakata, *Tetrahedron Lett.* **1982**, *23*, 229–232.
- [6] M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson, J. M. J. Williams, *J. Am. Chem. Soc.* **2009**, *131*, 1766–1774.
- [7] A. J. Watson, A. C. Maxwell, J. M. J. Williams, *J. Org. Chem.* **2011**, *76*, 2328–2331.
- [8] A. B. Enyong, B. Moasser, *J. Org. Chem.* **2014**, *79*, 7553–7563.
- [9] S. P. Shan, X. Xiaoke, B. Gnanaprakasam, T. T. Dang, B. Ramalingam, H. V. Huynh, A. M. Seayad, *RSC Adv.* **2015**, *5*, 4434–4442.
- [10] K. O. Marichev, J. M. Takacs, *ACS Catal.* **2016**, *6*, 2205–2210.
- [11] Q.-S. Xu, C. Li, Y. Xu, D. Xu, M.-H. Shen, H.-D. Xu, *Chin. Chem. Lett.* **2020**, *31*, 103–106.
- [12] Y. Tsuji, K.-T. Huh, Y. Ohsugi, Y. Watanabe, *J. Org. Chem.* **1985**, *50*, 1365–1370.
- [13] R. A. T. M. Abbenhuis, J. Boersma, G. van Koten, *J. Org. Chem.* **1998**, *63*, 4282–4290.
- [14] K. Fujita, T. Fujii, R. Yamaguchi, *Org. Lett.* **2004**, *6*, 3525–3528.
- [15] R. Yamaguchi, K. Fujita, T. Fujii, A. Komatsubara, Y. Enoki, *Heterocycles* **2007**, *74*, 673–682.
- [16] R. Yamaguchi, S. Kawagoe, C. Asai, K. Fujita, *Org. Lett.* **2008**, *10*, 181–184.
- [17] L. L. R. Lorentz-Petersen, L. U. Nordstrøm, R. Madsen, *Eur. J. Org. Chem.* **2012**, 6752–6759.
- [18] W. Zhang, X. Dong, W. Zhao, *Org. Lett.* **2011**, *13*, 5386–5389.
- [19] T. D. Apsunde, M. L. Trudell, *Synthesis* **2013**, *45*, 2120–2124.
- [20] a) O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden, J. M. J. Williams, *Chem. Commun.* **2010**, *46*, 1541–1543. b) O. Saidi, A. J. Blacker, G. W. Lamb, S. P. Marsden, J. E. Taylor, J. M. J. Williams, *Org. Process Res. Dev.* **2010**, *14*, 1046–1049.
- [21] R. Kawahara, K. Fujita, R. Yamaguchi, *Adv. Synth. Catal.* **2011**, *353*, 1161–1168.
- [22] Q. Zou, C. Wang, J. Smith, D. Xue, J. Xiao, *Chem. Eur. J.* **2015**, *21*, 9656–9661.
- [23] G. Cami-Kobeci, P. A. Slatford, M. K. Whittlesey, J. M. J. Williams, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 535–537.
- [24] K. Yuan, F. Jiang, Z. Sahli, M. Achard, T. Roisnel, C. Bruneau, *Angew. Chem. Int. Ed.* **2012**, *51*, 8876–8880.
- [25] R. Kawahara, K. Fujita, R. Yamaguchi, *J. Am. Chem. Soc.* **2010**, *132*, 15108–15111.
- [26] M. Larduinat, J. François, M. Jacolot, F. Popowycz, *J. Org. Chem.* **2023**, *88*, 7512–7517.
- [27] T. Yan, B. L. Feringa, K. Barta, *Nat. Commun.* **2014**, *5*, 5602.
- [28] T. Yan, B. L. Feringa, K. Barta, *ACS Catal.* **2016**, *6*, 381–388.
- [29] H.-J. Pan, T. W. Ng, Y. Zhao, *Chem. Commun.* **2015**, *51*, 11907–11910.
- [30] T. J. Brown, M. Cumbes, L. J. Diorazio, G. J. Clarkson, M. Wills, *J. Org. Chem.* **2017**, *82*, 10489–10503.
- [31] X. Bai, F. Aiolfi, M. Cettolin, U. Piarulli, A. Dal Corso, L. Pignataro, C. Gennari, *Synthesis* **2019**, *51*, 3545–3555.
- [32] P. Yang, C. Zhang, W.-C. Gao, Y. Ma, X. Wang, L. Zhang, J. Yue, B. Tang, *Chem. Commun.* **2019**, *55*, 7844–7847.
- [33] P. Melchiorre, M. Marigo, A. Carlone, G. Bartoli, *Angew. Chem. Int. Ed.* **2008**, *47*, 6138–6171
- [34] a) N. Srivastava, L. Macha, H.-J. Ha, *Org. Biomol. Chem.* **2020**, *18*, 5493–5512. b) Y. Lazib, J. G. Naves, A. Labande, P. Daubam, T. Saget, *ACS Org. Inorg. Au* **2023**, *3*, 120–129.
- [35] L. Miao, S. C. DiMaggio, H. Shu, M. L. Trudell, *Org. Lett.* **2009**, *11*, 1579–1582.
- [36] G. Bottari, A. Afanassenko, A. A. Castillo-Garcia, B. L. Feringa, K. Barta, *Adv. Synth. Catal.* **2021**, *363*, 5436–5442.
- [37] A. E. R. Chamberlain, K. J. Paterson, R. J. Armstrong, H. C. Twin, T. J. Donohoe, *Chem. Commun.* **2020**, *56*, 3563–3566.
- [38] Y. Liu, H. Diao, G. Hong, J. Edward, T. Zhang, G. Yang, B.-M. Yang, Y. Zhao, *J. Am. Chem. Soc.* **2023**, *145*, 5007–5016.
- [39] a) Y. Zhang, C.-S. Lim, D. S. B. Sim, H.-J. Pan, Y. Zhao, *Angew. Chem. Int. Ed.* **2014**, *53*, 1399–1403. b) C. S. Lim, T. T. Quach, Y. Zhao, *Angew. Chem. Int. Ed.* **2017**, *56*, 7176–7180.
- [40] P. Czodrowski, A. Mallinger, D. Wienke, C. Esdar, O. Pöschke, M. Busch, F. Rohdich, S. A. Eccles, M.-J. Ortiz-Ruiz, R. Schneider, F. I. Raynaud, P. A. Clarke, D. Musil, D. Schwarz, T. Dale, K. Urbahns, J. Blagg, K. Schiemann, *J. Med. Chem.* **2016**, *59*, 9337–9349.
- [41] R. D. Taylor, M. MacCoss, A. D. G. Lawson, *J. Med. Chem.* **2014**, *57*, 5845–5859.
- [42] For reviews on asymmetric BH reactions: a) T. Kwok, O. Hoff, R. J. Armstrong, T. J. Donohoe, *Chem. Eur. J.* **2020**, *26*, 12912–12926. b) K. Wang, M. Xiao, C. Wang, *Synlett* **2021**, *32*, 743–751. c) Y. Gao, G. Hong, B.-M. Yang, Y. Zhao, *Chem. Soc. Rev.* **2023**, *52*, 5541–5562.
- [43] Z. Shao, X. Zhang, X. Li, W. Wang, J. Ding, B. Cui, M. Zhao, *Chem. Eur. J.* **2023**, *29*, e202203758.
- [44] N. Hofmann, L. Homberg, K. C. Hultzsich, *Org. Lett.* **2020**, *22*, 7964–7970.
- [45] T. W. Ng, R. Tao, W. W. L. See, S. B. Poh, Y. Zhao, *Angew. Chem. Int. Ed.* **2023**, *62*, e202212528.