

## High-throughput screening of new Iron catalysts for Enantioselective Reductions by Online ESI-MS

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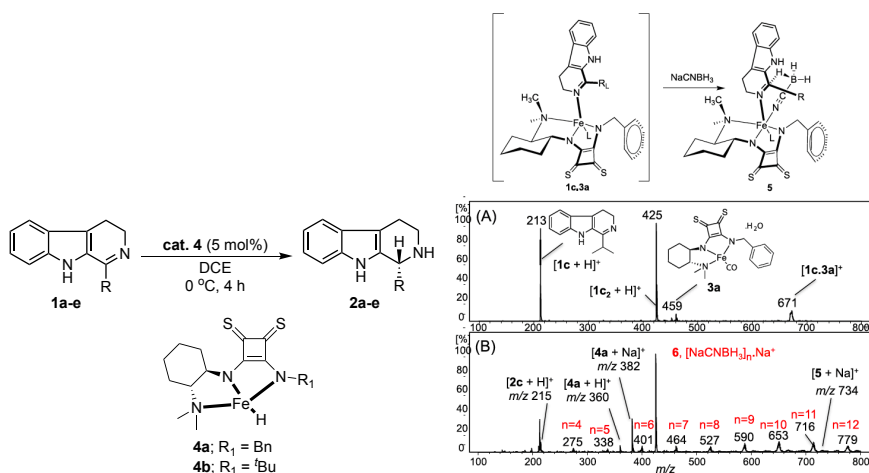
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### ABSTRACT

Assisted by high-throughput Electrospray Ionization Mass Spectrometry (ESI-MS/MS) screening, we developed chiral Fe-thiosquaramide catalysts (Fe-TSQ) **4** for the enantioselective imine reduction of dihydro- $\beta$ -carboline (DHBC) to chiral tetrahydro- $\beta$ -carbolines (**2**-THBCs). Chiral aryl and alkyl **2** were isolated in excellent yields and enantioselectivities up to 98 and ee 99%, respectively, employing 5-15 mol% of Fe-TSQ as catalyst.<sup>1-2</sup> ESI-MS is an important technique for mechanistic studies of chemical reactions in solution covering homogeneously catalyzed reactions.<sup>3</sup> Online high-throughput screening by ESI-MS gave a very clean spectrum displaying two Fe-containing cationic species, which spread the development of catalysts **4** (Figure 1A). When NaCNBH<sub>3</sub> was employed as source of hydride, species **6** was observed that explained why imines **1** were not concomitantly reduced by free borohydride in a non Fe-catalytic manner, which would afford (+/-)-**2** and decreasing %ee, but in fact **6** might be acting as a hydride source for formation of active Fe-complex intermediate **5**.<sup>4</sup>



**Figure 1.** Proposed mechanism based on high-throughput ESI-MS monitoring of the reaction of **1c** and **3a** with NaCNBH<sub>3</sub> in DCE. (A) First, a complex between **3a** and **1c** was observed. (B) By adding NaCNBH<sub>3</sub>, **5** was intercepted and **1c** reduced to **2c** after 3–30 min.

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### REFERENCES

- [1] Sathish, M.; Nachtigall, F. M.; Santos, L. S. *Org. Lett.* **2022**, *24*, 7627.
- [2] Sathish, M.; Nachtigall, F. M.; Santos, L. S. *RSC Adv.* **2020**, *10*, 38672.
- [3] Santos, L. S. *Reactive Intermediates: MS Investigations in Solution*; Wiley-VCR, **2010**.
- [4] Plaza-Lozano, D.; Ramírez-Palma, D.; Vela, A.; Olguín, J. *New J. Chem.* **2022**, *46*, 14910.