



HAL
open science

Iron-Catalyzed Enantioselective Intramolecular Inverse Electron-Demand Hetero Diels–Alder Reactions: An Access to Bicyclic Dihydropyran Derivatives

Jimmy Lauberteaux, Aurélien Lebrun, Arie van Der Lee, Marc Mauduit, Renata Marcia de Figueiredo, Jean-Marc Campagne

► **To cite this version:**

Jimmy Lauberteaux, Aurélien Lebrun, Arie van Der Lee, Marc Mauduit, Renata Marcia de Figueiredo, et al.. Iron-Catalyzed Enantioselective Intramolecular Inverse Electron-Demand Hetero Diels–Alder Reactions: An Access to Bicyclic Dihydropyran Derivatives. *Organic Letters*, 2019, 21 (24), pp.10007-10012. 10.1021/acs.orglett.9b03752 . hal-02429682

HAL Id: hal-02429682

<https://hal.science/hal-02429682>

Submitted on 23 Nov 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Iron Catalyzed Enantioselective Intramolecular Inverse Electron-Demand Hetero Diels-Alder Reactions: An Access to Bicyclic Dihydropyran Derivatives

Jimmy Lauberteaux,^a Aurélien Lebrun,^b Arie van der Lee,^c Marc Mauduit,^d Renata Marcia de Figueiredo,^a and Jean-Marc Campagne^{a*}

^a Institut Charles Gerhardt Montpellier, UMR 5253, Univ Montpellier, CNRS, ENSCM, Ecole Nationale Supérieure de Chimie, 240 Avenue Emile Jeanbrau, 34296 Montpellier Cedex 5 (France).

^b NMR Analysis: LMP, IBMM, Univ Montpellier, Montpellier, France.

^c X-Ray Structures Analysis: Institut Européen des Membranes (IEM), UMR 5632, Univ Montpellier, CNRS - Place Eugène Bataillon, 34095 Montpellier Cedex 5, France.

^d Univ Rennes, Ecole Nationale Supérieure de Chimie de Rennes, CNRS, ISCR UMR 6226, F-35000 Rennes, France.

KEYWORDS: Hetero Diels-Alder, Iron catalysis, Enantioselective catalysis

ABSTRACT: A highly enantioselective iron-catalyzed Intramolecular Inverse Electron-Demand Hetero Diels-Alder (IIEDHDA) reaction is reported. By using a chiral semicorrin ligand in the presence of 2,6 lutidine, good isolated yields and excellent enantioselectivities were observed (up to 96% ee). Thanks to the versatile post-functionalization of the acyl-imidazole moiety, this methodology represents a unique example of the straightforward construction of highly valuable enantioenriched bicyclic dihydropyran derivatives.

Among the powerful synthetically rich Diels-Alder family reactions,¹ the intermolecular catalytic asymmetric [4+2] Inverse Electron-Demand Hetero Diels-Alder (IEDHDA) reaction gained a considerable success notably to access the prevalent 3,4-dihydropyran core.² In contrast, very few examples have been reported that demonstrate high levels of enantiocontrol in the Intramolecular Inverse Electron-Demand Hetero Diels-Alder (IIEDHDA) reaction. Narasaka first explored this transformation with unsaturated oxazolidinone **1** in the presence of a stoichiometric amount of (Taddol)TiCl₂. Unfortunately, despite high enantioselectivities, a mixture of Alder-ene **2** and IIEDHDA **3** products was formed (Scheme 1, a).³ In a series of papers, Tietze developed efficient domino Knoevenagel Hetero Diels-Alder from aldehydes and 1,3-dicarbonyl compounds.⁴ In the presence of an excess of diacetoneglucose-derived titanium catalyst, the IIEDHDA products **5** were obtained in good yields and *cis* diastereoselectivities with moderate to good enantioselectivities (30-88% ee, Scheme 1, b). Wada described a catalytic enantioselective domino transesterification/intramolecular Diels-Alder sequence affording the *trans*-fused hydropyranopyrans **6** in good yields and excellent diastereo- and enantioselectivities (69-76% yield, 97-98% ee, Scheme 1, c), with albeit narrow scope (3 examples).⁵

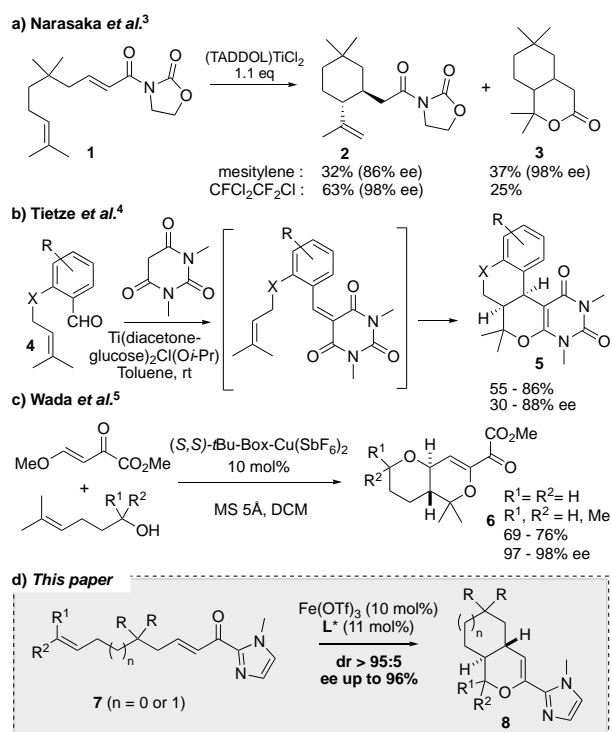
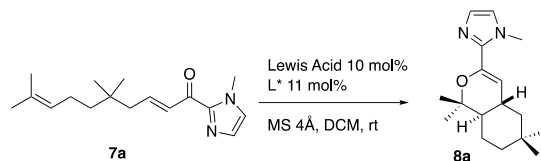


Figure 1. Enantioselective Intramolecular Inverse Electron-Demand Hetero Diels-Alder reactions.

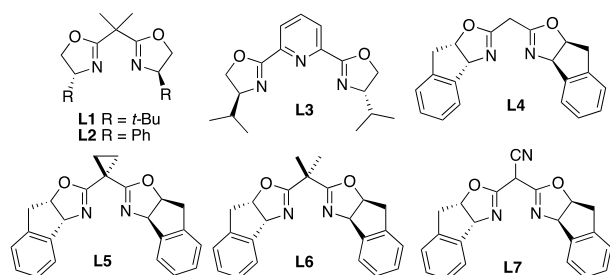
We would like to describe herein highly selective iron-catalyzed IEDHDA reactions starting from unsaturated acyl-imidazoles derivatives **7** (Scheme 1, d). Iron is an abundant, non-toxic, and inexpensive element and thus iron catalysis meets the requirements for sustainable and green chemistry.⁶

Based on our experience in asymmetric conjugate addition to unsaturated acyl-imidazoles,⁷ we were keen to exploit the unique properties of these ester/amide surrogates in IEDHDA reactions.⁸ Investigations began with the IEDHDA reaction of citral derivative **7a** using several Lewis acids in the absence of chiral ligands (see Supplementary Information, SI, for details). Among the diverse metal salts tested, Cu(OTf)₂ and Fe(OTf)₃ proved to be the more promising ones leading to the IEDHDA product **8a** as a single diastereomer in 69 and 83% yields respectively (table 1, entries 1,2). Interestingly, only traces (< 5%) of the Alder-ene product **9a** could be detected. As determined by ¹H NMR and further confirmed on X-Ray structures on post-transformed compounds (*vide infra*), **8a** adopts a bicyclic *trans* junction as expected through a sterically favored *anti* TS usually observed for *E*-dienes.^{2a-b}

Table 1. Chiral ligand optimization



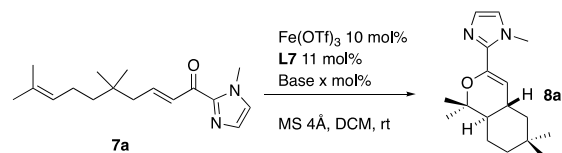
entry	LA	L*	time (h)	yield (%)	ee (%)
1	Cu(OTf) ₂	-	20	69	-
2	Fe(OTf) ₃	-	20	83	-
3	Fe(OTf) ₃	L1	19	42	0
4	Fe(OTf) ₃	L2	20	50	8
5	Fe(OTf) ₃	L3	18	35	8
6	Cu(OTf) ₂	L1	72	47	10
7	Cu(OTf) ₂	L3	20	39	5
8	Fe(OTf) ₃	L4	72	56	8
9	Fe(OTf) ₃	L5	72	48	53
10	Fe(OTf) ₃	L6	72	79	20
11	Cu(OTf) ₂	L4	72	27	14
12	Cu(OTf) ₂	L5	72	26	3
13	Cu(OTf) ₂	L6	72	48	6
14	Fe(OTf) ₃	L7	72	68	57



It is noteworthy that no reaction occurs when Weinreb amide or ethyl ester derivatives are involved, illustrating the peculiar properties of the acyl-imidazole. Indeed, acyl-imidazoles are more electron-withdrawing groups compared to esters and other ester-surrogates, and they are able via a double mode of coordination to warrant a defined transition state.⁸

Asymmetric reactions were thus next explored with Cu(OTf)₂ and Fe(OTf)₃ in the presence of most commonly used Box and Pybox **L1-L6** ligands with however disappointing results (Table 2, entries 3-13).⁹ The notable exception was observed with Fe(OTf)₃/L5 (entry 9) for which a 53% ee could be reached. All our further attempts to improve the selectivity by changing the reaction parameters (solvent, temperature, iron salts) proved anyway unsuccessful in our hands. It was anticipated that the presence of an electron withdrawing group on the bridging carbon of the bis(oxazoline) could enhance the reactivity of the metal complex.¹⁰ This was confirmed by using L7 bearing a cyano group that produced the compound **8a** in 68% isolated yield and improved 57% ee (entry 14). Anticipating that traces of triflic acid could promote a parallel and racemic catalytic cycle, the use of a base as additive was envisioned in the presence of Fe(OTf)₃/L7 (Table 2).¹¹

Table 2. Base as additive in the asymmetric IEDHDA reaction with 7a



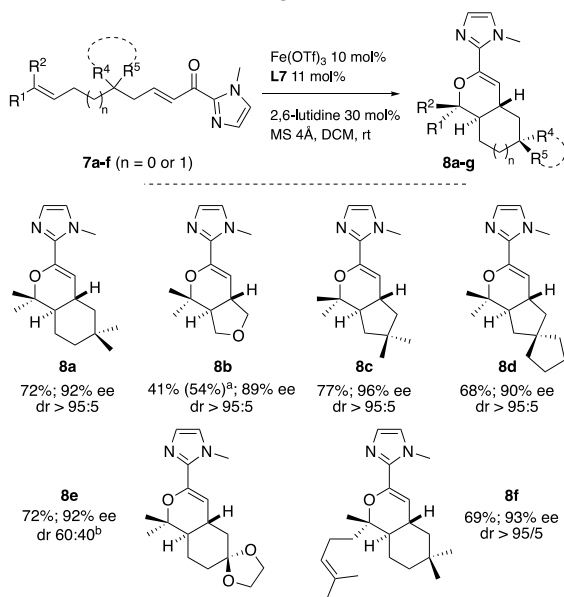
entry	base (mol %)	time (h)	yield (%)	ee (%)
1	-	72	68	57
2	DIPEA (20)	72	35	6
3	DABCO (15)	72	25	11
4	2,6-di- <i>t</i> -butylpyridine (30)	72	64	75
5	2,6-di- <i>t</i> -butyl-4-methylpyridine (30)	72	71	86
6	2,6-lutidine-4-hydroxy (30)	72	89	72
7	2,4,6-collidine (30)	72	72	85
8	2,6-lutidine (30)	72	72	92
9	2,6-lutidine (30)	72	52	52
<i>with L5</i>				
10	2,6-lutidine (30)	72	63	45
<i>without MS 4Å</i>				

After a screening of several bases, a drastic improvement of enantioselectivity was observed with pyridine derivatives (entries 4-8) reaching a maximum of 92% ee in the presence of 2,6 lutidine (30 mol%). Some other interesting observations could be drawn from the optimization study.

First, enantioselectivity dropped to 52% when using other chiral ligands such as **L5** (entry 9). Second, the molecular sieves appeared essential to maintain the enantioselection (63% yield, 45% ee, entry 10). At last, the catalyst can also be *in-situ* generated from FeCl₃ and AgOTf with similar good results (see Supplementary Information, SI, for details).

After optimization of the IIEDHDA reaction with citral derivative **7a**, the general scope was next explored (Scheme 1). When the chain length (6-6 vs 6-5 bicycles) was changed or bearing different substituents on the R⁴/R⁵ positions (alkyl chains, heteroatom or an acetal group), the reaction provided expected bicyclic compounds **8a-e** in good yields and stereoselectivities (dr >95:5; 89%-96% ee) with the exception of **8e** (dr 60:40). In this case, both separable diastereomers could be obtained in 92% ee. Concerning the 5,6-fused ring systems (compounds **8b-d**), the *trans* configuration could be ascertained by analyzing the H₄ NMR signal (H close to the double bond at the ring junction): For example in **8b**, the signal is a dddd with coupling constants of 12.1; 11.1; 7.2 and 2.0 Hz. The attribution of each coupling constant is as followed: 12.1 (H₄-H_{bicyclic}), 11.1 (H₄-CH_{trans}H'), 7.2 (H₄-CHH'_{cis}), 2.0 (H₄-H_{alkene}). The large coupling constant is consistent with a *trans* relationship along the ring junction. Finally, we also observed that substrate **7f** possessing a farnesyl chain (R¹ ≠ R²) afforded product **8f** in 69% yield as a single diastereomer (dr > 95:5) and high enantioselectivity (93% ee).

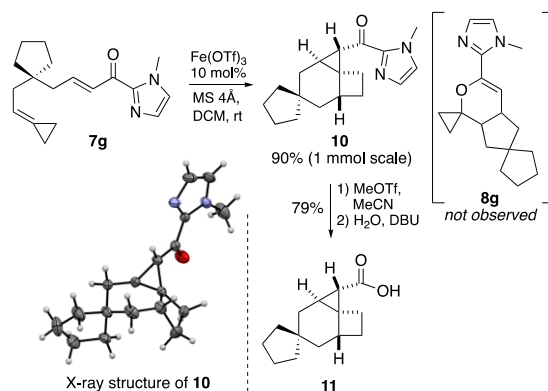
Scheme 1. Scope of the asymmetric IIEDHDA reaction



^a 15 mol% of Fe(OTf)₃ were used. ^b 92% ee was also observed for the minor *cis* diastereomer.

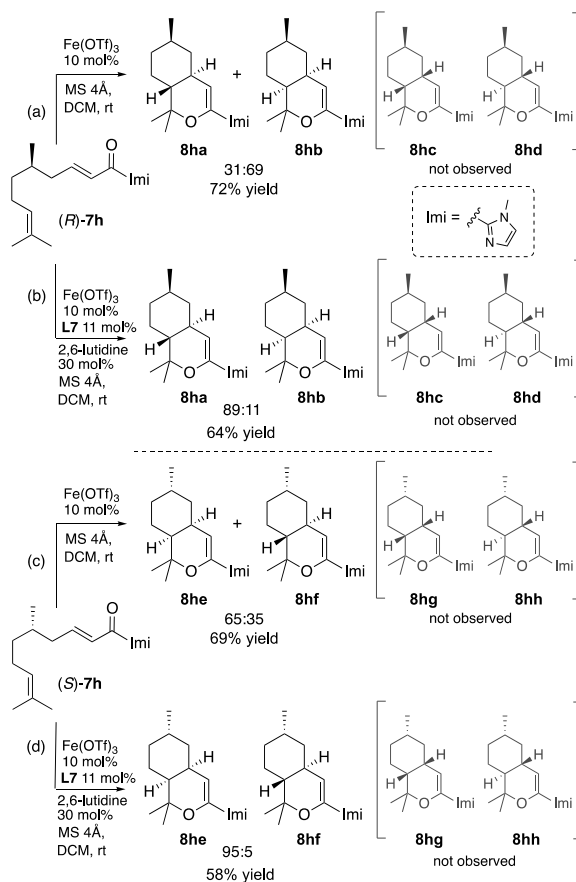
A more surprising result was observed with compounds **7g** bearing a remote cyclopropylidene unit. The IIEDHDA product **8g** was not observed and compound **10** was isolated in 90% yield (1 mmol scale) as a single diastereomer. The structure of **10** is rather complex embedding 3-, 4-, 5- (spiro) and 6-membered cycles (Scheme 2). Structural determination proved challenging and was finally ascertained using a ¹³C NMR INADEQUATE sequence (see SI).

Scheme 2. Rearrangement of **7g** in IIEDHDA reaction conditions



Its structure was unambiguously confirmed by single crystal X-Ray diffraction studies. Moreover, the acyl-imidazole was further easily transformed into the corresponding carboxylic acid **11** in 79% yield.⁸ Finally, in the presence of L7-lutidine, compound **10** could be isolated in 85% yield and 37% ee. The formation of **10** can tentatively be explained through two successive Wagner-Meerwein rearrangements (See mechanistic proposal in SI).

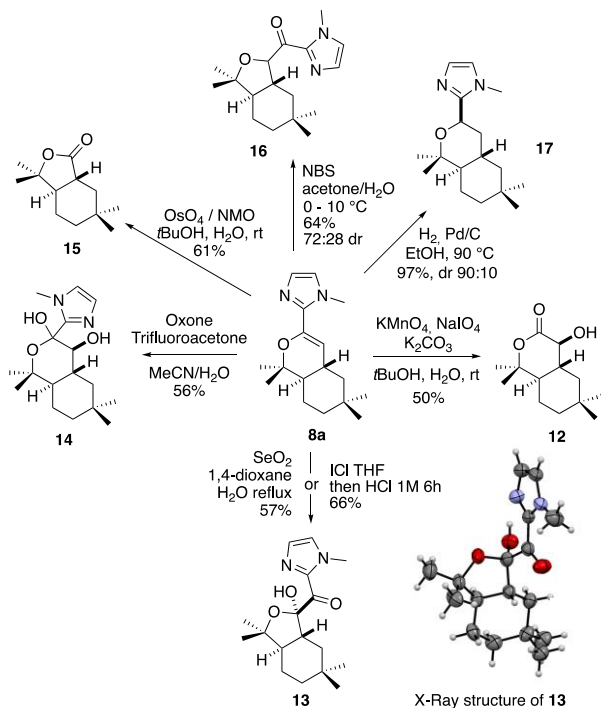
Scheme 3. IIEDHDA reaction with (*R*)- and (*S*)-enantiomer of citronellal derivative **7h**



We next turned our attention to citronellal derivatives **7h** bearing a methyl group in the δ position (Scheme 3).

These substrates are more challenging because the introduction of a stereogenic center could potentially lead to 4 diastereomers and induce match/mismatch pairs. Moreover, they lack beneficial Thorpe-Ingold effect. Starting from the (*R*) enantiomer, the IEDHDA reaction was first carried out in the absence of chiral ligand (Scheme 3, a). In this case, only two diastereomers **8ha** and **8hb** were observed in a 31:69 ratio by ¹H NMR on the crude material. Moving to the optimized enantioselective conditions, a reverse 89:11 ratio could be observed (Scheme 3, b). The structure of the major diastereomer **8ha** could be unambiguously confirmed by ¹H NMR NOESY experiments (for the determination of the structure of minor diastereomers, see SI). With the (*S*) enantiomer under achiral conditions (Fe(OTf)₃, DCM, rt), two other diastereomers **8he** and **8hf** were observed in a 65:35 ratio (determined by ¹H NMR on the crude material, Scheme 3, c). In chiral conditions (Fe(OTf)₃, **L7**, lutidine), an improved 95:5 ratio of the same two diastereomers **8he** and **8hf** could be observed with 58% isolated yield (Scheme 3, d). The structure of **8he** proved more difficult to establish. From NMR studies (see SI), it appears that **8he** adopts a bicyclic *cis* junction, with the two protons at the ring junction being *cis* to the stereogenic methyl group. These two experiences highlight the prominent role of chiral ligand **L7** in the double stereodifferentiation with these chiral substrates. The scale-up reaction was next attempted on acyl-imidazoles **7a** and (*S*)-**7h**. Moving from a 0.2 to 1.0 mmol scale was found experimentally more practical and beneficial in terms of isolated yield (84% vs 72% and 90% vs 58% respectively) with no change in the stereoselectivity (enantio- or diastereoselectivity) issues.

Scheme 4. IEDHDA products post-functionalization



The IEDHDA products **8** possess an usual bicyclic structure with a pending imidazolyl group and thus offer many possibilities for synthetic post-transformations. Acid-mediated direct transformation of the imidazole ring (or the imidazolium salt after methylation with MeOTf) in **8a** proved unsuccessful under various conditions. We thus next explored conditions for the double bond oxidation. In the presence of $\text{KMnO}_4/\text{NaIO}_4$, the α -hydroxy lactone **12** was obtained in 50% yield as a single diastereomer. The oxidation of **8a** in the presence of SeO_2 led to the corresponding diketone isolated as the acetal **13** as a single diastereomer. The structure was ascertained by an X-Ray analysis and also confirmed the *trans* relationship of the two hydrogens at the ring junction. Interestingly, the same compound **13** could be obtained from **8a** using ICl in 66% yield. Epoxidation of the double bond was next attempted out using oxone and trifluoroacetone,¹² but compound **14** resulting from a dihydroxylation reaction was obtained in 56% yield as a single diastereomer. By using OsO_4/NMO , lactone **15** was isolated in 61% yield. In the presence of NBS, the ring contraction product **16** was obtained in 64% yield in a 72:28 dr. Finally, the enol ether double bond could be reduced in the presence of Pd/C to give compound **17** in 97% yield (90:10 dr).

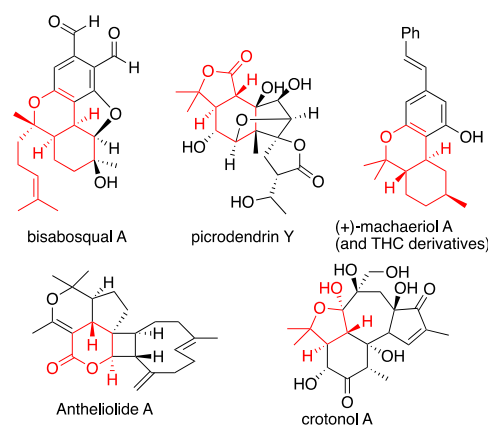
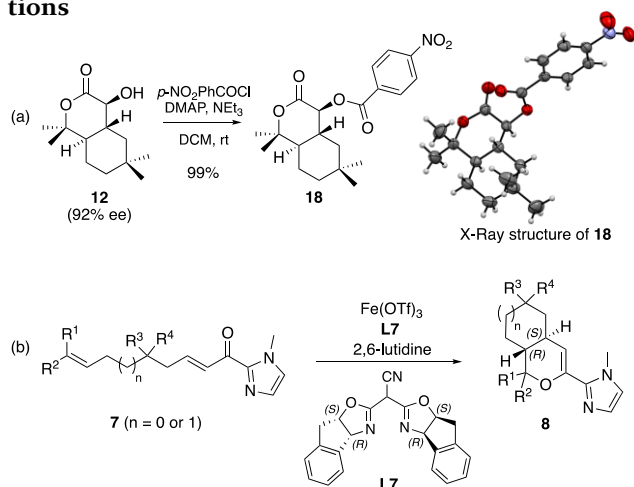


Figure 2. Natural Products embedding dihydropyran derivatives **8b** and post-transformed products **12-17**.

It should be emphasized that bicyclic dihydropyran derivatives **8** and post-transformed products **12-17** are present in a wide range of bioactive natural products, as illustrated in figure 2.¹³

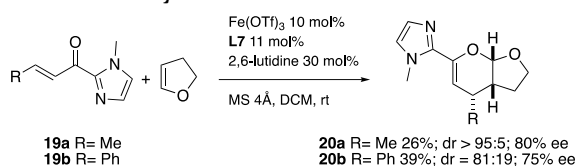
Scheme 5. Determination of the absolute configurations



The determination of absolute configurations of IEDHDA products **8** could be finally obtained via the derivatization of enantiomerically enriched **12** (92% ee) to the corresponding *p*-NO₂ phenyl ester **18** allowing the formation of a crystalline compound (Scheme 5, a). An X-ray structure for **18** was obtained confirming the relative stereochemistry determined by ¹H NMR but also establishing absolute configurations. It should be emphasized that this experiment confirms the absolute configurations observed in **8ha** (obtained from (*R*)-**7h**). Accordingly, the absolute stereochemistries for compounds **8** obtained from Fe(OTf)₃/L7 (obtained from (1*R*, 2*S*)-(+)-*cis*-1-amino-2-in-danol)) were thus tentatively assigned by analogy (Scheme 5, b).

Finally, an intermolecular version of the hetero Diels-Alder reaction of acyl-imidazoles **19** (R = Me or Ph) with dihydrofuran led to the Diels-Alder products **20** in low yields but promising enantioselectivities (Scheme 6).

Scheme 6. Asymmetric intermolecular reactions



In summary, we have developed a highly enantioselective iron-catalyzed Intramolecular Inverse Electron-Demand Hetero Diels-Alder (IEDHDA) reaction using C₂-symmetric semicorrin ligand and 2,6-lutidine. This iron-catalyzed reaction generates enantioenriched bicyclic dihydropyran derivatives in good yields and excellent diastereo- and enantio-selectivities. These compounds can be further easily transformed into a large range of valuable bicyclic heterocycles. Further mechanistic investigations and DFT calculations are currently ongoing in our laboratory to unveil the role of the base in these transformations, and determine the stepwise vs concerted character of this [4+2] cycloaddition, as we envision that this catalytic system will

inspire future studies in iron-catalyzed asymmetric transformations.

ASSOCIATED CONTENT

AUTHOR INFORMATION

Corresponding Author

* E-mail: jean-marc.campagne@enscm.fr

Author Contributions

The manuscript was written through contributions of all authors.

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

The project was supported by funds from the ENSCM, the CNRS and the *Fondation pour le développement de la chimie des substances naturelles et ses applications* (JL PhD grant). Special thanks to Takasago Company for a generous gift of citronellal.

REFERENCES

- (a) Corey, E. J. Catalytic Enantioselective Diels-Alder Reactions: Methods, Mechanistic Fundamentals, Pathways, and Applications. *Angew. Chem. Int. Ed.* **2002**, *41*, 1650–1667. (b) Juhl, M.; Tanner, D. Recent Applications of Intramolecular Diels-Alder Reactions to Natural Product Synthesis. *Chem. Soc. Rev.* **2009**, *38*, 2983–2992. (c) Heravi, M. M.; Vavari, V. F. Recent Applications of Intramolecular Diels-Alder Reaction in Total Synthesis of Natural Products. *RSC Advances* **2015**, *5*, 50890–50912.
- (a) Pałasz, A. Recent Advances in Inverse-Electron-Demand Hetero-Diels-Alder Reactions of 1-Oxa-1,3-Butadienes. *Top. Curr. Chem.* **2016**, *374*, 24. (b) Tietze L.F.; Ketschau G. Hetero Diels-Alder Reactions in Organic Chemistry. *Top. Curr. Chem.* **1997**, *189*, 1–120. (c) Jiang, X.; Wang, R. Recent Developments in Catalytic Asymmetric Inverse-Electron-Demand Diels-Alder Reaction. *Chem. Rev.* **2013**, *113*, 5515–5546. (d) Desimoni, G.; Faita, G.; Quadrelli, P. Forty Years after “Heterodiene Syntheses with α,β -Unsaturated Carbonyl Compounds”: Enantioselective Syntheses of 3,4-Dihydropyran Derivatives. *Chem. Rev.* **2018**, *118*, 2080–2248.
- (a) Narasaka, K.; Hayashi, Y.; Shimada, S. Asymmetric Intramolecular Ene Reaction Catalyzed by a Chiral Titanium Alkoxide. *Chem. Lett.* **1988**, *17*, 1609–1612. (b) Narasaka, K.; Hayashi, Y.; Shimada, S.; Yamada, J. Asymmetric Intramolecular Ene Reaction Catalyzed by a Chiral Titanium Reagent and Synthesis of (-)- ϵ -Cadinene. *Isr. J. Chem.* **1991**, *31*, 261–271.
- (a) Tietze, L. F.; Brumby, T.; Brand, S.; Bratz, M. Inter- and Intramolecular Hetero Diels-Alder Reactions, XXI. Intramolecular Hetero Diels-Alder Reaction of Alkylidene-1,3-Dicarbonyl Compounds. Experimental Evidence for an Asymmetric Transition State. *Chem. Ber.* **1988**, *121*, 499–506. (b) Tietze, L. F.; Brand, S.; Brumby, T.; Fennen, J. Intramolecular Hetero-Diels-Alder Reactions of Oxadienes: Influence of Substituents of the Tether on the Diastereoselectivity. *Angew. Chem. Int. Ed. Eng.* **1990**, *29*, 665–667. (c) Tietze, L. F.; Saling, P. Enantioselective Sequential Transformations by Use of Metal Complexes: Tandem-Knoevenagel-Hetero-Diels-Alder Reactions with New Chiral Lewis Acids. *Chirality* **1993**, *5*, 329–333. (d) Sabitha, G.; Fatima, N.; Reddy, E. V.; Yadav, J. S. First Examples of Proline-Catalyzed Domino Knoevenagel/Hetero-Diels-Alder/Elimination Reactions. *Adv. Synth. Catal.* **2005**, *347*, 1353–1355.

(5) Wada, E.; Koga, H.; Kumaran, G. A Novel Catalytic Enantioselective Tandem Transesterification–Intramolecular Hetero Diels–Alder Reaction of Methyl (*E*)-4-Methoxy-2-Oxo-3-Butenoate with δ,ϵ -Unsaturated Alcohols. *Tetrahedron Lett.* **2002**, *43*, 9397–9400.

(6) Pellissier, H. Recent developments in enantioselective iron-catalyzed transformations. *Coord. Chem. Rev.* **2019**, *386*, 1–31.

(7) (a) Drissi-Amraoui, S.; Morin, M. S. T.; Crévisy, C.; Baslé, O.; de Figueiredo, R. M.; Mauduit, M.; Campagne, J.-M. Copper-Catalyzed Asymmetric Conjugate Addition of Dimethylzinc to Acyl-N-methylimidazole Michael Acceptors: A Powerful Synthetic Platform. *Angew. Chem. Int. Ed.* **2015**, *54*, 11830–11834. (b) Drissi-Amraoui, S.; Schmid, T. E.; Lauberteaux, J.; Crévisy, C.; Baslé, O.; de Figueiredo, R. M.; Halbert, S.; Gérard, H.; Mauduit, M.; Campagne, J.-M. Copper-Catalyzed Asymmetric Conjugate Addition of Dimethylzinc to Acyl-N-methylimidazole Michael Acceptors: Scope, Limitations and Iterative Reactions. *Adv. Synth. Catal.* **2016**, *358*, 2519–2540. (c) Lauberteaux, J.; Crévisy, C.; Baslé, O.; de Figueiredo, R. M.; Mauduit, M.; Campagne, J.-M. Copper-Catalyzed Asymmetric Conjugate Additions of Bis(Pinacolato)Diboron and Dimethylzinc to Acyl-N-Methylimidazole Michael Acceptors: A Highly Stereoselective Unified Strategy for 1,3,5,...n (OH, Me) Motif Synthesis. *Org. Lett.* **2019**, *21*, 1872–1876.

(8) For seminal work in asymmetric catalysis, see: (a) Evans, D.A.; Fandrick, D. K.; Song, H.-J. Enantioselective Friedel–Crafts Alkylations of α,β -Unsaturated 2-Acyl Imidazoles Catalyzed by Bis(oxazolonyl)pyridine–Scandium(III) Triflate Complexes. *J. Am. Chem. Soc.* **2005**, *127*, 8942–8943. (b) Evans, D.A.; Fandrick, D. K. Catalytic Enantioselective Pyrrole Alkylations of α,β -Unsaturated 2-Acyl Imidazoles. *Org. Lett.* **2006**, *8*, 2249–2252. For reviews, see: (c) Lauberteaux, J.; Pichon, D.; Baslé, O.; Mauduit, M.; de Figueiredo, R. M.; Campagne, J.-M. Acyl-Imidazoles: A Privileged Ester Surrogate for Enantioselective Synthesis. *ChemCatChem* **2019**, *11*, doi: 10.1002/cctc.201900754. (d) Mansot, J., Vasseur, J.-J.; Arseniyadis, S.; Smietana, M. α,β -Unsaturated 2-Acyl-Imidazoles in Asymmetric Biohybrid Catalysis. *ChemCatChem* **2019**, *11*, doi: 10.1002/cctc.201900743.

(9) (a) Johnson, J. S.; Evans, D. A. Chiral Bis(Oxazoline) Copper(II) Complexes: Versatile Catalysts for Enantioselective Cycloaddition, Aldol, Michael, and Carbonyl Ene Reactions. *Acc. Chem. Res.* **2000**, *33*, 325–335. (b) Ollevier, T. Iron bis(oxazoline) complexes in asymmetric catalysis. *Catal. Sci. Technol.* **2016**, *6*, 41–48.

(10) (a) Pfaltz, A. Chiral Semicorrins and Related Nitrogen Heterocycles as Ligands in Asymmetric Catalysis. *Acc. Chem. Res.* **1993**, *26*, 339–345. (b) Nolin, K. A.; Ahn, R. W.; Kobayashi, Y.; Kennedy-Smith, J. J.; Toste, F. D. Enantioselective Reduction of Ketones and Imines Catalyzed by (CN-Box)ReV–Oxo Complexes. *Chem. – A Eur. J.* **2010**, *16*, 9555–9562.

(11) The exact role of the added base is not yet understood. Efforts to crystallize the Fe(OTf)₃/L7 or Fe(OTf)₃/L7/2,6-lutidine catalytic systems were unsuccessful in our hands only leading to the crystalline L7·TfOH salt, catalytically inactive in the absence of iron.

(12) Yang, D.; Wong, M.-K.; Yip, Y.-C. Epoxidation of Olefins Using Methyl(Trifluoromethyl)Dioxirane Generated in Situ. *J. Org. Chem.* **1995**, *60*, 3887–3889.

(13) (a) Green, D.; Carmely, S.; Benayahu, Y.; Kashman, Y. Antheliolide A & B: Two New C₂₄-Acetoacetylated Diterpenoids of the Soft Coral *Anthelia Glauca*. *Tetrahedron Lett.* **1988**, *29*, 1605–1608. (b) Smith, A. B.; Carroll, P. J.; Kashman, Y.; Green, D. Revised Structures of Antheliolides A and B. *Tetrahedron Lett.* **1989**, *30*, 3363–3364. (c) Wang, J.; Qin, L.; Zhao, B.; Cai, L.; Zhong, Z.; Liu, Y.; Zhou, X. Crotonols A and B, Two Rare Tiglane Diterpenoid Derivatives Against K562 Cells from *Croton Tiglium*. *Org. Biomol. Chem.* **2019**, *17*, 195–202. (d) Muhammad, I.; Li, X.-C.; Dunbar, D. C.; ElSohly, M. A.; Khan, I. A. Antimalarial (+)-*trans*-Hexahydrodibenzopyran Derivatives from *Machaerium Multiflorum*. *J. Nat. Prod.* **2001**, *64*, 1322–1325. (e) Minagawa, K.; Kouzuki, S.; Nomura, K.; Kawamura, Y.; Tani, H.; Terui, Y.; Nakai, H. Bisabosquols, Novel Squalene Synthase Inhibitors. *J. Antibiot.* **2001**, *54*, 890–895. (f) Suzuki, Y.; Koike, K.; Nagahisa, M.; Nikaido, T. New Picrotoxane Terpenoids from *Picrodendron Baccatum*. *Tetrahedron* **2003**, *59*, 6019–6025.