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Synthesis of chiral hydantoin derivatives by homogeneous Pd-catalyzed asymmetric hydrogenation

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ABSTRACT

5-Aryl substituted chiral hydantoin derivatives were synthesized via asymmetric hydrogenation of prochiral exocyclic alkenes using a Pd/BINAP catalyst. Moderate to good enantioselectivity were obtained (21–90% ee). A chiral Brönsted acid additive was found to be a key factor to obtain high enantioselectivity.

1. Introduction

Chiral hydantoin derivatives are widespread among natural products and have shown great potential application in the area of pharmaceuticals (Fig. 1).[1] These compounds have been also used as chiral catalysts and auxiliaries.[2] Up to now, several methodologies have been developed to obtain these molecules, including enzymatic synthesis, resolution and chiral pool approaches.[3] These methods, however, often suffer from low efficiency and poor economy. Thus developing a new catalytic asymmetric synthesis method is important.

Asymmetric hydrogenation of hydantoin derived exocyclic alkene is one of the most direct methods to obtain the target chiral molecules. Although great success has been achieved in the metal catalyzed homogeneous asymmetric hydrogenation of various alkenes, imines, and ketones,[4] the prochiral exocyclic alkene substrates remains less studied.[5] Before our research, there was no report on the homogeneous asymmetric hydrogenation of hydantoin derived exocyclic alkenes. Compared with the acyclic and endocyclic unsaturated substrates, exocyclic alkenes are difficult to form catalyst–substrate complexes due to the ring hindrance, which has been certified as a key factor to achieve high enantioselectivity.[6] Recently, Zhang et al. reported a new approach to synthesise chiral succinimide derivatives with excellent yields and ee values (up to 99% ee) by using Ir/BiphPHOX catalysts.[7] Ding et al. reported a highly effective method to obtain medium-sized cyclic carbonyl compounds bearing an α-stereogenic carbon center by using Ir/SpinPhox catalysts. A broad range of exocyclic alkenes were successfully hydrogenated with excellent enantiomeric excess (up to 98% ee).[8] In general, despite great success being made in the asymmetric hydrogenation of exocyclic alkenes, exploring a new catalyst system and extending substrates ranges still remains a great challenge.

Over the past fifteen years, Pd complexes have gradually been demonstrated as effective catalysts in homogeneous asymmetric hydrogenation,[9] especially in the asymmetric hydrogenation of imines, enamines and heteroarenes.[10] Herein, we report the first asymmetric hydrogenation of hydantoin derived exocyclic alkenes using a Pd/BINAP catalyst (Fig. 2).

2. Results and discussion

The reaction conditions investigated are listed in Table 1. The reaction took place in 2,2,2-trifluoroethanol (TFE) with only 5% ee (entries 1–6).[11] Both the conversion and enantioselectivity could be improved by increasing the reaction temperature (entries 6–8). When the hydrogen gas pressure was increased, there is only a subtle influence on the reaction conversion and selectivity (entries 8–10).

In order to improve the catalytic activity and selectivity, we screened a series of additives. It was reported by Zhou et al. that a chiral Brönsted acid additive is crucial to achieve high enantioselectivity in the Pd-catalyzed asymmetric hydrogenation of unprotected indoles.[12] Inspired by their work, we screened several chiral Brönsted acids (Fig. 3).

We found that the reaction was obviously promoted by Brönsted acid (entries 11–15). When two equivalents (compared with catalyst) D-CSA acid were added, the conversion was 100%

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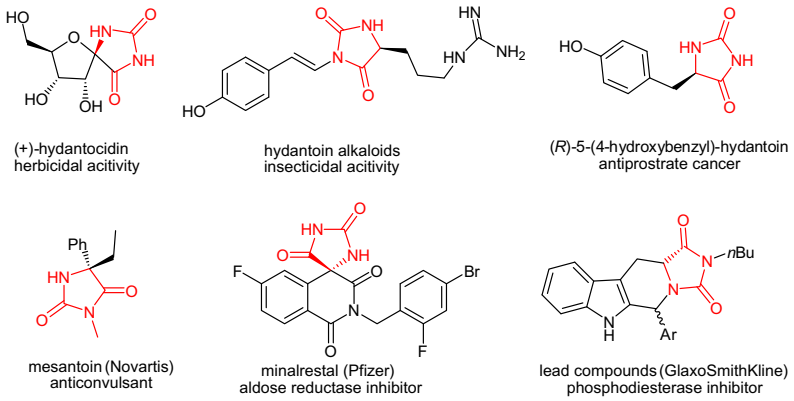


Figure 1. Chiral hydantoin derivatives with bioactivity.

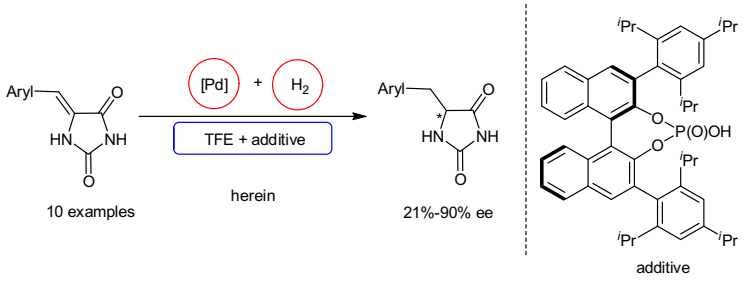


Figure 2. Pd catalyzed asymmetric hydrogenation of exocyclic alkene.

and the enantioselectivity was raised to 33% ee. When the same amount L-CSA was added, the ee value of the product decreased to 9%. This phenomenon was probably due to the mismatch between the chiral catalyst and the chiral additive. We also screened several BINOL-derived phosphoric acid additives. It was found that the starting material was completely converted into the desired product and the ee value increased using this type additive (entries 13–15). When (*R*)-BP3 was utilized, the ee value was reached up to 45%. The absolute configuration was determined as (*S*) by comparing the specific rotation with the literature sign. In this case, the (*R*)-catalyst was matched with the (*R*)-additive. It is worth mentioning that the enantioselectivity of the product decreased when the additive exceeded or was less than two equivalents (entries 15, 17 and 18).

We also screened several different chiral phosphine ligand catalysts (entries 19–23). Except for (*R*,*R*)-DIOP-Pd catalyst, the other catalysts all showed high catalytic activity. The enantioselectivity was influenced by the different catalysts. For the (*R*,*R*)-DIOP-Pd catalyst, only 30% ee was obtained. For the (*R*)-SegPhos-Pd catalyst, 44% ee was obtained, which was similar to the (*R*)-BINAP-Pd catalyst.

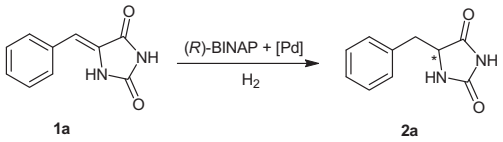
Encouraged by these promising results obtained in the hydrogenation of alkene **1a**, a variety of other hydantoin derived exocyclic alkenes were examined under the optimized conditions (Table 2). The substituents on the aryl ring had a significant influence on the enantioselectivity. Substrates with an electron donating group showed much better enantioselectivity than those with an electron withdrawing group (entries 1–4). For example, the *para*-methoxy product was obtained with 63% ee while the *para*-bromo product was only 21% ee (entries 2 and 3). When the same substituent was attached to the *meta*- or *ortho*-position of the phenyl ring, the enantioselectivity was clearly superior to the *para*-substituted product (53% ee, 51% ee *vs* 26% ee, entries 4–6).

With these experimental results in hand, we speculated that the electron donating group close to the double bond was probably helpful with regards to the enantioselectivity. We synthesized several substrates with electron donating group on the *ortho* position of the phenyl ring. As expected, we found moderate to excellent ee were obtained by using this type substrate. For the *ortho*-methyl and *ortho*-methoxy substituted substrates, 90% ee and 88% ee were obtained respectively (entries 7, 8). However, when the group changed from methoxy to ethoxy or *n*-butoxy, much lower ee were obtained (entries 9, 10).

To elucidate the mechanism of the Pd-catalyzed asymmetric hydrogenation of hydantoin derived exocyclic alkene in the presence of Brönsted acid, ^{1}H NMR and isotopic labelling experiments were carried out. Under the optimized conditions of the asymmetric hydrogenation, only 4% equivalents (*R*)-BP3 compared with the substrate was added. ^{1}H NMR showed that there was no obvious difference between the **1a** with or without the (*R*)-BP3 except for the NH proton. Even when 30% equivalent (*R*)-BP3 was added, there was still no obvious difference. These results indicated that the substrate could be protonated by (*R*)-BP3. However, tautomerization between the enamine and imine was not observed. Moreover, **1a** was hydrogenated in D_2 with the (*R*)-BINAP-Pd catalyst (Fig. 4). Deuterium at the 5-position of hydantoin ring was not observed. However one deuterium was found in benzyl position. These results confirmed that the carbon–carbon double bond was asymmetrically hydrogenated rather than the carbon–nitrogen double bond in our experiment.

To the best of our knowledge, this is the first example of a homogeneous Pd-catalyzed highly enantioselective synthesis of

Table 1
Optimizing the hydrogenation conditions of **1a**[a]



Entry	Solvent	*T* (°C)	Additive	Conv. (%)[b]	ee (%)[c]
1	Methanol	**25**	No	<5	N.d.
2	DCM	**25**	No	<5	N.d.
3	Toluene	**25**	No	<5	N.d.
4	THF	**25**	No	<5	N.d.
5	Acetone	**25**	No	<5	N.d.
6	TFE	**25**	No	20	5
7	TFE	**40**	No	25	11
8	TFE	**70**	No	60	22
9[d]	TFE	**70**	No	58	20
10[e]	TFE	**70**	No	63	24
11	TFE	**70**	(*D*)-CSA	>95	33
12	TFE	**70**	(*L*)-CSA	>95	9
13	TFE	**70**	(*R*)-BP1	>95	40
14	TFE	**70**	(*R*)-BP2	>95	41
15	TFE	**70**	(*R*)-BP3	>95	45
16[f]	TFE	**70**	(*R*)-BP3	>95	1
17[g]	TFE	**70**	(*R*)-BP3	>95	41
18[h]	TFE	**70**	(*R*)-BP3	>95	43
19[i]	TFE	**70**	(*R*)-BP3	61	30
20[j]	TFE	**70**	(*R*)-BP3	>95	44
22[k]	TFE	**70**	(*R*)-BP3	>95	41
23[l]	TFE	**70**	(*R*)-BP3	>95	40

[a] Reaction conditions: 0.05 mmol substrate in 2.0 mL solvent, 40 atm H_2, substrate/catalyst = 50, 0.002 mmol additive, 24 h.
[b] Based on ^{1}H NMR analysis of the crude product.
[c] Determined by HPLC with a chiral column.
[d] 10 atm H_2.
[e] 60 atm H_2.
[f] (*S*)-BINAP-Pd catalyst.
[g] 0.001 mmol additive.
[h] 0.003 mmol additive.
[i] (*R*,*R*)-DIOP-Pd catalyst.
[j] (*R*)-SegPhos-Pd catalyst.
[k] (*R*)-MeO-BIPHEP-Pd catalyst.
[l] (*R*)-SynPhos-Pd catalyst.

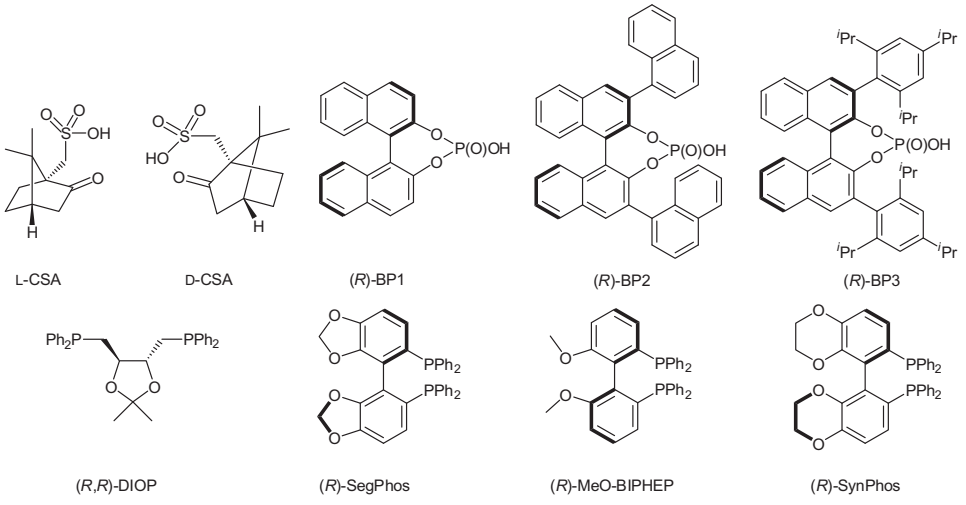


Figure 3. Chiral Brönsted acids additives and chiral ligands.

hydantoin derivatives by hydrogenation. A detailed reaction mechanism of this reaction and the asymmetric hydrogenation of 5-alkyl substituted substrates are currently underway in our laboratory.

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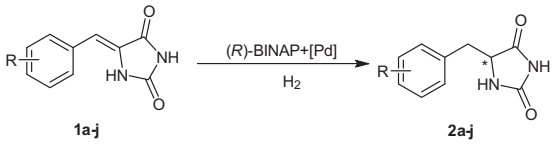
Table 2
Asymmetric hydrogenation of exocyclic alkene **1**[a]



Entry	R	Yield (%)[b]	ee (%)[c]
1	4-H	95	45 (*S*)
2	4-MeO	96	63
3	4-Br	96	21
4	4-Cl	93	26
5	3-Cl	94	53
6	2-Cl	91	51
7	2-MeO	89	88
8	2-Me	92	90
9	2-EtO	88	56
10	2-^{n}BuO	88	61

[a] Reaction conditions: 0.05 mmol substrate in 2.0 mL TFE, substrate/catalyst = 50, 40 atm H_2, 70 °C, 0.002 mmol additive, 24 h.
[b] Isolated yield.
[c] Determined by HPLC with a chiral column.

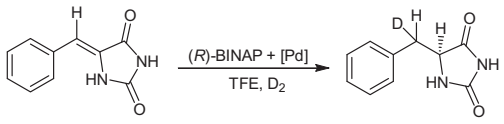


Figure 4. Asymmetric hydrogenation of **1a** with **D2**.

3. Conclusion

In conclusion, we have developed an efficient catalytic system for the enantioselective synthesis of chiral hydantoin derivatives. Moderate to good enantioselectivities were obtained (21–90% ee). Chiral Brönsted acid additive was found to be a key figure to achieve high enantioselectivity.

4. Experimental

4.1. General

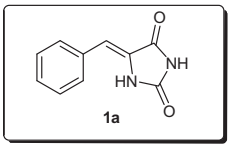
Unless otherwise noted, all experiments were carried out under an inert atmosphere of dry argon by using standard Schlenk-type techniques. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Model Avance DMX 400 Spectrometer (^{1}H NMR 300 or 500 MHz and ^{13}C NMR 125 MHz) respectively. Chemical shifts (δ) were given in ppm and were referenced to residual solvent or TMS peaks. All other chemicals were used as received from Aldrich or Acros without further purification.

4.2. General procedure for the synthesis of substrates

4.2.1. General procedure

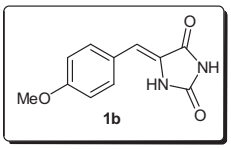
A 250 mL flask was charged with hydantoin (10.0 g, 100 mmol), aromatic aldehyde (100 mmol), ethanolamine (3.05 g, 50 mmol) and 100 mL of solvent (ethnol/water = 1/1, *v*/*v*). The reaction mixture was then heated and stirred at reflux for 24 h. After cooling to room temperature, a large amount of crystals were formed. The mixture was filtered and the filter cake was washed with 20 mL of cold ethanol. The crystals were then collected and dried under reduced pressure.

4.2.1.1. (*Z*)-5-Benzylideneimidazolidine-2,4-dione 1a.



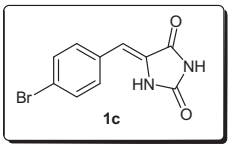
Yield: 85%; Colorless crystal, mp = 224.0–225.1 °C; ^{1}H NMR (300 MHz, d^{6}-DMSO) δ (ppm): 6.41 (s, 1H), 7.32–7.43 (m, 3H), 7.63 (t, *J* = 1.5 Hz, 2H), 10.52 (br s, 1H), 11.18 (br s, 1H); ^{13}C NMR (125 MHz, d^{6}-DMSO) δ (ppm): 166.0, 156.1, 133.4, 129.8, 129.2, 128.8, 128.4, 108.7.

4.2.1.2. (*Z*)-5-(4-Methoxybenzylidene)imidazolidine-2,4-dione 1b.



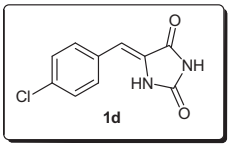
Yield: 87%; Pale yellow crystal, mp >250.0 °C; ^{1}H NMR (300 MHz, d^{6}-DMSO) δ (ppm): 3.80 (s, 3H), 6.39 (s, 1H), 6.93–6.98 (m, 2H), 7.56–7.60 (m, 2H), 10.39 (br s, 1H), 11.12 (br s, 1H); ^{13}C NMR (125 MHz, d^{6}-DMSO) δ (ppm): 166.0, 159.9, 156.1, 131.5, 126.5, 125.9, 114.7, 109.1, 55.7.

4.2.1.3. (*Z*)-5-(4-Bromobenzylidene)imidazolidine-2,4-dione 1c.



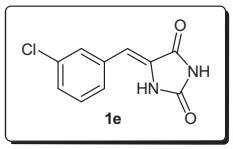
Yield: 89%; Colorless crystal, mp >250.0 °C; ^{1}H NMR (300 MHz, d^{6}-DMSO) δ (ppm): 6.38 (s, 1H), 7.57 (s, 4H), 10.58 (br s, 1H), 11.25 (br s, 1H); ^{13}C NMR (125 MHz, d^{6}-DMSO) δ (ppm): 165.9, 156.1, 132.7, 132.1, 131.7, 129.0, 121.9, 107.3.

4.2.1.4. (*Z*)-5-(4-Chlorobenzylidene)imidazolidine-2,4-dione 1d.



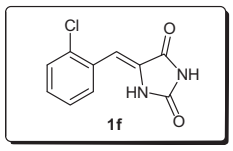
Yield: 88%; Colorless crystal, mp >250.0 °C; ^{1}H NMR (300 MHz, d^{6}-DMSO) δ (ppm): 6.40 (s, 1H), 7.42–7.46 (m, 2H), 7.61–7.66 (m, 2H), 10.60 (br s, 1H), 11.21 (br s, 1H); ^{13}C NMR (125 MHz, d^{6}-DMSO) δ (ppm): 165.9, 156.1, 133.2, 132.4, 131.5, 129.2, 128.9, 107.2.

4.2.1.5. (*Z*)-5-(3-Chlorobenzylidene)imidazolidine-2,4-dione 1e.



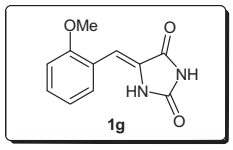
Yield: 90%; Colorless crystal, mp = 243.2–244.0 °C; ^{1}H NMR (300 MHz, d^6-DMSO) δ (ppm): 6.56 (s, 1H), 7.32–7.41 (m, 2H), 7.51–7.54 (m, 1H), 7.70–7.73 (m, 1H), 10.65 (br s, 1H), 11.31 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 165.7, 156.1, 133.5, 131.3, 130.6, 130.5, 130.3, 130.1, 128.0, 103.3.

4.2.1.6. (*Z*)-5-(2-Chlorobenzylidene)imidazolidine-2,4-dione 1f.



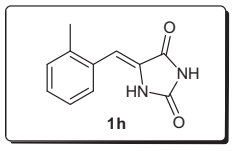
Yield: 83%; Colorless crystal, mp >250.0 °C; ^{1}H NMR (300 MHz, d^6-DMSO) δ (ppm): 6.39 (s, 1H), 7.35–7.44 (m, 2H), 7.54–7.57 (m, 1H), 7.70 (s, 1H), 10.69 (br s, 1H), 11.27 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 165.8, 156.2, 135.6, 134.1, 130.9, 129.5, 129.0, 128.5, 106.9.

4.2.1.7. (*Z*)-5-(2-Methoxybenzylidene)imidazolidine-2,4-dione 1g.



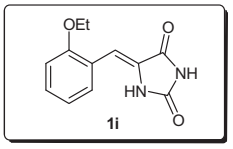
83%; Pale yellow crystal, mp = 224.3.2–225.0; ^{1}H NMR (300 MHz, d^6-DMSO) δ (ppm): 3.84 (s, 3H), 6.65 (s, 1H), 6.95–7.05 (m, 2H), 7.30–7.35 (m, 1H), 7.57–7.61 (m, 1H), 10.72 (br s, 2H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 166.0, 157.6, 156.0, 130.5, 129.7, 128.4, 121.9, 121.0, 111.6, 103.2, 56.1.

4.2.1.8. (*Z*)-5-(2-Methylbenzylidene)imidazolidine-2,4-dione 1h.



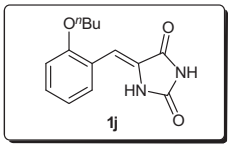
Yield: 87%; Colorless crystal, mp = 247.8–248.9 °C; ^{1}H NMR (300 MHz, d^6-DMSO) δ (ppm): 2.32 (s, 3H), 6.48 (s, 1H), 7.20–7.25 (m, 3H), 7.50–7.53 (m, 1H), 10.45 (br s, 1H), 11.17 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 165.9, 156.1, 137.4, 132.2, 130.7, 129.3, 129.0, 128.8, 126.7, 106.2, 20.0.

4.2.1.9. (*Z*)-5-(2-Ethoxybenzylidene)imidazolidine-2,4-dione 1i.



Yield: 81%; Colorless crystal, mp = 219.4–220.7 °C; ^{1}H NMR (300 MHz, d^6-DMSO) δ (ppm): 1.37 (t, J = 6.9 Hz, 3H), 4.06–4.13 (m, 2H), 6.66 (s, 1H), 6.93–7.04 (m, 1H), 7.27–7.33 (m, 1H), 7.57–7.60 (m, 1H), 7.58 (dd, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 1H), 10.31 (br s, 1H), 11.15 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 166.0, 156.9, 155.9, 130.5, 129.8, 128.4, 122.0, 120.9, 112.4, 103.4, 64.1, 15.0.

4.2.1.10. (*Z*)-5-(2-Butoxybenzylidene)imidazolidine-2,4-dione 1j.



Yield: 79%; Colorless crystal, mp = 197.8–198.1 °C; ^{1}H NMR (300 MHz, d^6-DMSO) δ (ppm): 0.94 (t, J = 7.2 Hz, 3H), 1.40–1.52 (m, 2H), 1.69–1.79 (m, 2H), 4.04 (t, J = 6.6 Hz, 2H), 6.67 (s, 1H), 6.93–6.98 (m, 1H), 7.02–7.05 (m, 1H), 7.27–7.33 (m, 1H), 7.59 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 10.32 (br s, 1H), 11.15 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 166.0, 157.0, 155.9, 130.4, 129.7, 128.4, 122.1, 120.9, 112.5, 103.2, 68.1, 31.2, 19.2, 14.1.

4.3. General procedure for the asymmetric hydrogenation

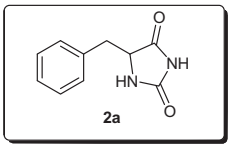
4.3.1. General procedure for the preparation of the catalyst

At first, (*R*)-BINAP (68.4 mg, 0.11 mmol) and Pd(OCOCF$_3$)$_2$ (33.2 mg, 0.10 mmol) were placed in a dried Schlenk tube under a nitrogen atmosphere, after which 5 mL of degassed anhydrous acetone were added. The mixture was stirred at room temperature for 1 h, then the solvent was removed under vacuum to give the catalyst.

4.3.2. General procedure for the asymmetric hydrogenation

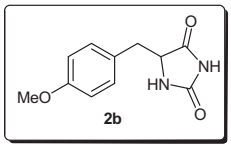
In a 10 mL glass-lined stainless steel reactor with a magnetic stirring bar with substrate (0.05 mmol), the above prepared Pd-catalyst (1×10^{-3} mmol), additive (2×10^{-3} mmol) and 2 mL of TFE were added. The autoclave was closed and then pressurized with H_2 to 40 atm. The mixture was stirred at 70 °C for 24 h. After carefully venting of the hydrogen, the reaction solvent was removed under reduced pressure. The crude product was used to determine the conversion and enantioselectivity.

4.3.2.1. (5-Benzylimidazolidine-2,4-dione 2a.



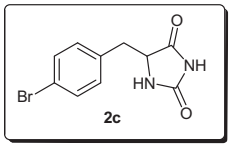
Yield: 95%; White solid, mp = 183.9–184.0 °C; $[\alpha]_D^{20} = -36.0$ (*c* 0.1, TFE) for 46% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 2.57–3.40 (m, 2H), 4.40 (t, *J* = 5.0 Hz, 1H), 7.25–7.37 (m, 5H), 7.98 (br s, 1H), 10.49 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 175.7, 157.7, 136.1, 130.3, 128.6, 127.2, 59.0, 37.0; HPLC: (OH-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 16.1 min, t_2 = 19.2 min.

4.3.2.2. (5-(4-Methoxybenzyl)imidazolidine-2,4-dione 2b.



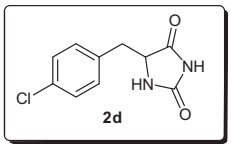
Yield: 96%; White solid, mp = 180.0–182.3 °C; $[\alpha]_D^{20} = -27.0$ (*c* 0.1, TFE) for 63% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 2.86 (d, *J* = 5.0 Hz, 1H), 3.71 (s, 3H), 4.27 (t, *J* = 5.0 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 7.87 (br s, 1H), 10.38 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 175.7, 158.5, 157.6, 131.2, 127.8, 114.0, 59.0, 55.4, 35.9. HPLC: (OD-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 20.2 min, t_2 = 23.3 min.

4.3.2.3. (5-(4-Bromobenzyl)imidazolidine-2,4-dione 2c.



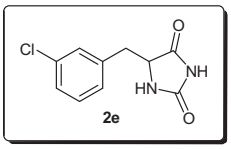
Yield: 96%; Yellow solid, mp >250 °C; $[\alpha]_D^{20} = -10.0$ (*c* 0.1, TFE) for 21% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 2.86–2.94 (m, 2H), 4.33 (t, *J* = 5.0 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.92 (br s, 1H), 10.46 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm):175.5, 157.5, 135.5, 132.4, 131.4, 120.5, 58.6, 36.2. HPLC: (OD-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 16.6 min, t_2 = 19.1 min.

4.3.2.4. (5-(4-Chlorobenzyl)imidazolidine-2,4-dione 2d.



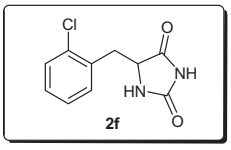
Yield: 93%; White solid, mp = 202.7–203.0 °C; $[\alpha]_D^{20} = -50.0$ (*c* 0.1, TFE) for 26% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 2.97–3.04 (m, 2H), 4.42 (t, *J* = 5.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.99 (br s, 1H), 10.55 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 175.5, 157.6, 135.1, 132.0, 131.9, 131.5, 129.2, 128.5, 58.7, 36.2. HPLC: (OD-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 15.8 min, t_2 = 17.7 min.

4.3.2.5. (5-(3-Chlorobenzyl)imidazolidine-2,4-dione 2e.



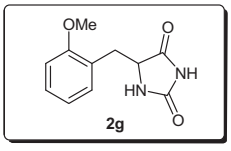
Yield: 94%; White solid, mp >250.0 °C; $[\alpha]_D^{20} = +18.0$ (*c* 0.1, TFE) for 53% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 2.97–3.06 (m, 2H), 4.44 (t, *J* = 4.5 Hz, 1H), 7.23 (d, *J* = 6.5 Hz, 3H), 7.336 (s, 1H), 7.38–7.42 (m, 2H), 8.02 (br s, 1H), 10.54 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 175.5, 157.6, 138.7, 133.1, 130.4, 130.0, 128.9, 127.2, 58.6, 36.5. HPLC: (OD-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 17.2 min, t_2 = 19.7 min.

4.3.2.6. (5-(2-Chlorobenzyl)imidazolidine-2,4-dione 2f.



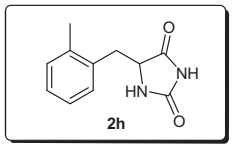
Yield: 91%; White solid, mp = 201.5–202.0 °C; $[\alpha]_D^{20} = -25.0$ (*c* 0.1, TFE) for 51% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 3.00–3.04 (m, 1H), 3.26–3.30 (m, 1H), 4.41 (t, *J* = 6.0 Hz, 1H), 7.36–7.38 (m, 2H), 7.43–7.44 (m, 1H), 7.51–7.53 (m, 1H), 7.98 (br s, 1H), 10.72 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 175.6, 157.8, 134.6, 133.9, 132.4, 129.7, 129.1, 127.6, 57.7, 35.5; HPLC: (OD-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 21.4 min, t_2 = 24.9 min.

4.3.2.7. (5-(2-Methoxybenzyl)imidazolidine-2,4-dione 2g.



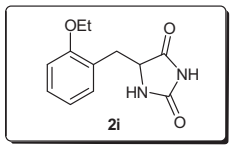
Yield: 89%; White solid, mp = 189.1–190.2 °C; $[\alpha]_D^{20} = -105.0$ (*c* 0.1, TFE) for 88% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 2.70–2.74 (m, 1H), 3.05–3.09 (m, 1H), 3.77 (s, 3H), 4.24 (t, *J* = 5.5 Hz 1H), 6.85–6.88 (m, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 6.5 Hz, 1H), 7.22 (t, *J* = 7.0 Hz, 1H), 7.24 (br s, 1H), 10.53 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 176.0, 157.9, 157.8, 131.4, 128.6, 124.9, 120.6, 111.1, 57.9, 55.8, 32.8. HPLC: (OD-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 17.8 min, t_2 = 19.9 min.

4.3.2.8. (5-(2-Methylbenzyl)imidazolidine-2,4-dione 2h.



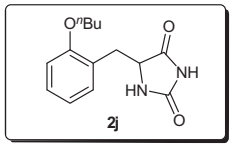
Yield: 92%; White solid, mp = 215.2–215.3 °C; $[\alpha]_D^{20} = -125.0$ (c 0.1, TFE) for 88–90% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 2.36 (s, 3H), 2.92–2.96 (m, 1H), 3.07–3.11 (m, 1H), 4.37–4.40 (m, 1H), 7.18–7.25 (m, 4H), 7.99 (br s, 1H), 10.62 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 176.0, 157.8, 137.0, 135.2, 130.5, 130.4, 127.1, 126.1, 58.6, 19.9. HPLC: (AD-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 12.3 min, t_2 = 13.4 min.

4.3.2.9. (5-(2-Ethoxybenzyl)imidazolidine-2,4-dione 2i.



Yield: 88%; White solid, mp >250 °C; $[\alpha]_D^{20} = -27.0$ (c 0.1, TFE) for 56% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 1.34 (t, J = 7.0 Hz, 3H), 2.70–2.72 (m, 1H), 3.04–3.08 (m, 1H), 4.00–4.04 (m, 2H), 4.25–4.27 (m, 1H), 6.85 (t, J = 7.5 Hz, 1H), 6.93–6.94 (m, 1H), 7.13–7.14 (m, 1H), 7.18–7.21 (m, 1H), 7.71 (br s, 1H), 10.53 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 176.0, 157.8, 157.1, 131.4, 128.5, 125.0, 120.5, 111.9, 63.6, 57.9, 32.9, 15.1; HPLC: (OJ-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 16.3 min, t_2 = 18.5 min.

4.3.2.10. (5-(2-Butoxybenzyl)imidazolidine-2,4-dione 2j.



Yield: 88%; Brown solid, mp >250 °C; $[\alpha]_D^{20} = -30.0$ (c 0.1, TFE) for 61% ee; ^{1}H NMR (500 MHz, d^6-DMSO) δ (ppm): 0.94 (t, J = 7.5 Hz, 3H), 1.44–1.48 (m, 2H), 1.71–1.74 (m, 2H), 2.68–2.72 (m, 1H), 3.05–3.09 (m, 1H), 3.94–3.97 (m, 2H), 4.22–4.25 (m, 1H), 6.85 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 8.5, Hz 1H), 7.13–7.15 (m, 1H), 7.18–7.21 (m, 1H), 7.73 (br s, 1H), 10.55 (br s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ (ppm): 176.0, 157.8, 157.2, 131.4, 128.5, 125.1, 120.5, 111.9, 67.6, 57.9, 33.1, 31.3, 19.3, 14.2. HPLC: (AS-H, elute: Hexane/^{i}PrOH = 90/10, detector: 210 nm, flow rate: 1.0 mL/min), t_1 = 25.9 min, t_2 = 34.3 min.

Acknowledgments

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A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetasy.2016.10.006.

References

1. For selected reviews, see: (a) Manuela, M.; Michael, G. *Org. Prep. Proced. Int.* **2004**, *36*, 391–443; (b) Ware, E. *Chem. Rev.* **1950**, *46*, 403–470; (c) Hofreiter, M.; Serre, D.; Poinar, H. N.; Kuch, M.; Paabo, S. *Nat. Rev. Genet.* **2001**, *2*, 353–359.
2. For selected examples, see: (a) Zhai, Z.; Chen, J.; Wang, H.; Zhang, Q. *Synth. Comm.* **2003**, *33*, 1873–1883; (b) Metallinos, C.; John, J.; Nelson, J.; Dudding, T.; Belding, L. *Adv. Synth. Catal.* **2013**, *355*, 1211–1219; (c) Li, X. R.; Lu, C. F.; Chen, Z. X.; Li, Y.; Yang, G. C. *Tetrahedron: Asymmetry* **2012**, *23*, 1380–1384.
3. For selected examples, see: (a) Kartozoa, I.; Kanyonyo, M.; Happaerts, T.; Lambert, D. M.; Scriba, G. K. E.; Chankvetadze, B. *J. Pharm. Biomed. Anal.* **2002**, *27*, 457–465; (b) May, O.; Verseck, S.; Bommarius, A.; Drauz, K. *Org. Process Res. Dev.* **2002**, *6*, 452–457; (c) Maiti, B.; Chanda, K.; Sun, C. M. *Org. Lett.* **2009**, *11*, 4826–4829; (d) Zhang, D.; Xing, X.; Cuny, G. D. *J. Org. Chem.* **2006**, *71*, 1750–1753; (e) Barta, N. S.; Sidler, D. R.; Somerville, K. B.; Weissman, S. A.; Larsen, R. D.; Reider, P. J. *Org. Lett.* **2000**, *2*, 2821–2824.
4. For selected reviews, see: (a) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994; (b) Xie, J. H.; Zhu, S. F.; Zhou, Q. L. *Chem. Rev.* **2011**, *111*, 1713–1760; (c) Wang, D. S.; Chen, Q. A.; Lu, S. M.; Zhou, Y. G. *Chem. Rev.* **2012**, *112*, 2557–2590; (d) Verendel, J. J.; Pàmies, O.; Diéguez, M.; Andersson, P. G. *Chem. Rev.* **2014**, *114*, 2557–2590; (e) Yoshimura, M.; Tanaka, S.; Kitamura, M. *Tetrahedron Lett.* **2014**, *55*, 3635–3640; (f) Wang, D.; Hou, C.; Chen, L.; Liu, X.; An, Q.; Hu, X. *Chin. J. Org. Chem.* **2013**, *33*, 1355–1368.
5. For selected examples, see: (a) Ohta, T.; Miyake, T.; Seido, N.; Kumobayashi, H.; Takaya, H. *J. Org. Chem.* **1995**, *60*, 357–363; (b) Yue, T.; Nugent, W. A. *J. Am. Chem. Soc.* **2002**, *124*, 13692–13693; (c) Chung, J. Y. L.; Zhao, D.; Hughes, D. L.; McNamara, J. M.; Grabowski, E. J. J.; Reider, P. J. *Tetrahedron Lett.* **1995**, *36*, 7379–7382; (d) Yamamoto, T.; Orura, M.; Amano, A.; Adachi, K.; Hagiwara, T.; Kanisawa, T. *Tetrahedron Lett.* **2002**, *43*, 9081–9084.
6. For selected reviews and examples, see: (a) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106–122; (b) Chan, A. S. C.; Pluth, J. J.; Halpern, J. *J. Am. Chem. Soc.* **1980**, *102*, 5952–5954; (c) Xie, J. H.; Zhou, Q. L. *Acta Chim. Sinica* **2012**, *70*, 1427–1438.
7. (a) Liu, Y. Y.; Zhang, W. B. *Angew. Chem., Int. Ed.* **2013**, *52*, 2203–2206; (b) Liu, Y. Y.; Gridnev, I. D.; Zhang, W. B. *Angew. Chem., Int. Ed.* **2014**, *53*, 1901–1905.
8. Liu, X.; Han, Z.; Wang, Z. B.; Ding, K. L. *Angew. Chem., Int. Ed.* **2014**, *53*, 1978–1982.
9. For selected reviews, see: (a) Chen, Q. A.; Ye, Z. S.; Duan, Y.; Zhou, Y. G. *Chem. Soc. Rev.* **2013**, *42*, 497–511; (b) Tietze, L. F.; Ila, H.; Bell, H. P. *Chem. Rev.* **2004**, *104*, 3453–3516.
10. For selected examples, see: (a) Abe, H.; Amii, H.; Uneyama, K. *Org. Lett.* **2001**, *3*, 313–315; (b) Wang, D. S.; Wang, D. W.; Zhou, Y. G. *Synlett* **2011**, 947–950; (c) Duan, Y.; Li, L.; Chen, M. W.; Yu, C. B.; Fan, H. J.; Zhou, Y. G. *J. Am. Chem. Soc.* **2014**, *136*, 7688–7700; (d) Yu, C. B.; Gao, K.; Wang, D. S.; Shi, L.; Zhou, Y. G. *Chem. Commun.* **2011**, 5052–5054.
11. For selected examples, see: (a) Cahard, D.; Bizet, V. *Chem. Soc. Rev.* **2013**, *42*, 497–511; (b) Suzuki, A.; Mae, M.; Amii, H.; Uneyama, K. *J. Org. Chem.* **2004**, *69*, 5132–5134; (c) Sugiishi, T.; Matsugi, M.; Hamamoto, H.; Amii, H. *RSC Adv.* **2015**, *5*, 17269–17282.
12. For selected examples, see: (a) Zhou, X. Y.; Wang, D. S.; Bao, M.; Zhou, Y. G. *Tetrahedron Lett.* **2011**, *52*, 2826–2829; (b) Zhou, X. Y.; Bao, M.; Zhou, Y. G. *Adv. Synth. Catal.* **2011**, *353*, 84–88; (c) Wang, D. S.; Chen, Q. A.; Li, W.; Yu, C. B.; Zhou, Y. G.; Zhang, X. *J. Am. Chem. Soc.* **2010**, *132*, 8909–8911.