EurJOC
European Journal of Organic Chemistry

A Journal of ChemPubSoc Europe

Accepted Article

Title: Iron- and Zinc-mediated Synthetic Approach to Enantiopure Dihydroquinoxalinones

Authors: Dazhi Li and Thierry Ollevier

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201801639

Link to VoR: http://dx.doi.org/10.1002/ejoc.201801639

Supported by ACES Asian Chemical Editorial Society

WILEY-VCH

10.1002/ejoc.201801639

FULL PAPER

WILEY-VCH

Iron- and Zinc-mediated Synthetic Approach to Enantiopure Dihydroquinoxalinones

Dazhi Li,[a] and Thierry Ollevier*[a]

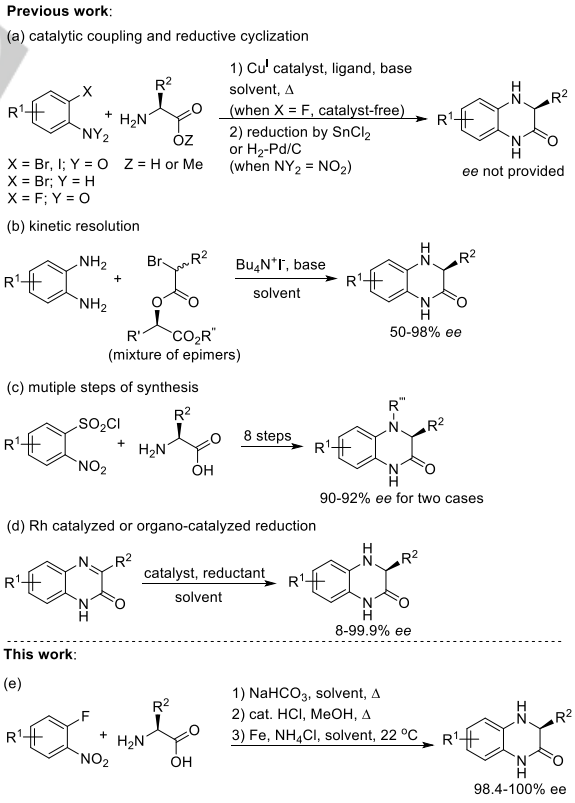
Abstract: A general and efficient synthesis of enantiopure dihydroquinoxalinones has been developed using naturally occurring amino acids as starting materials. The reductive cyclization of *N*-(*o*-nitroaryl)amino esters was performed by using iron and zinc metal under mild conditions in a water/ethyl acetate mixture. The corresponding dihydroquinoxalinones were obtained in moderate to high yields and high enantiomeric purity, among which 7 new compounds were unprecedented in the literature.

Introduction

As the core structure of many pharmaceuticals and biologically active compounds, quinoxalinone derivatives serve as important building blocks in drug synthesis and agrochemistry.[1] Non-nucleoside HIV-1 reverse transcriptase inhibitor GW420867X[2] is a good example of chiral drugs with the dihydroquinoxalinone core. In addition, dihydroquinoxalinone motifs are present in bromodomain inhibitors,[3] cholesteryl ester transfer protein inhibitors,[4] antagonists of the selective human A3 adenosine receptor[5] and other non-nucleoside reverse transcriptase inhibitors.[6] Hence, the synthesis of dihydroquinoxalinones has attracted considerable attention in the past decades, and remains of great interest today.[7]

Several methods have been reported for the synthesis of chiral dihydroquinoxalinones.[8] The first method involved the coupling of *o*-nitroaryl- or *o*-aminoaryl halides with natural amino acids (Scheme 1a).[8a, 8b] *o*-Nitroaryl bromides/iodides and *o*-aminoaryl bromides were coupled with amino acids using a Cu^I catalyst, followed by reduction and cyclization. By using *o*-aminoaryl bromides, the reaction conditions were harsh.[8b] In these two cases, the requirement of air-sensitive catalysts, toxic organic solvents and ligands was a major disadvantage. More frequently, *o*-nitroaryl fluorides were reacted through S_NAr with amino acids[8i-q] or their esters[8r-t] using a base without catalyst. Subsequently, the nitro group was reduced by H_2,[8o] $SnCl_2$,[8n] Zn,[8s] Fe,[8m] or $Na_2S_2O_4$.[8p] The drawbacks of the methods using H_2 or $SnCl_2$ are the use of expensive noble Pd catalyst or toxic Sn pollutants, respectively. When Zn and Fe were employed, the reactions suffered from narrow scopes with low to moderate yields, and because of the harsh conditions of the reductive cyclization, up to 10% of dihydroquinoxalinone was potentially racemized.[8r] When $Na_2S_2O_4$ was employed in water, the yield was low as well. The second method used the kinetic resolution of α-bromoacid esters with diaminobenzenes (Scheme 1b).[8c-g] However, the enantiopurity varied for each of the obtained compounds. Moreover, various toxic organic solvents, such as MeCN and CH_2Cl_2, were used. The third method used solid-phase synthesis starting from *o*-nitrobenzenesulfonyl chloride (Scheme 1c)[8h] and numerous steps were necessary. The fourth method emerged in recent years involving asymmetric catalysis using rhodium,[1, 8z] Lewis bases,[7b, 8aa] Brønsted acids[8y] and Lewis acids[7a] as catalysts (Scheme 1d). Despite the good results disclosed, most studies were run in non-environmentally-benign organic solvents.[9] Also, the fact that the ligands were expensive or not commercially available and the reaction required inert atmosphere or produced toxic waste made these methods problematic.[10]

So far, there has been no general method using Fe for the synthesis of chiral dihydroquinoxalinones from amino acids under benign conditions. Thus, using Fe as reagent for both the reduction and the cyclization steps leaves space for milder conditions to be explored, since Fe is an abundant, cheap,[11] and non-toxic element.[12] Herein, we report a new approach for the synthesis of enantiopure dihydroquinoxalinones with an expanded scope of substrates (Scheme 1e). The final products were obtained in high yields by reductive cyclization using Fe as reductant in a H_2O/EtOAc solvent at room temperature. All reactions were carried out under air.



Scheme 1. Synthetic routes of chiral dihydroquinoxalinones.

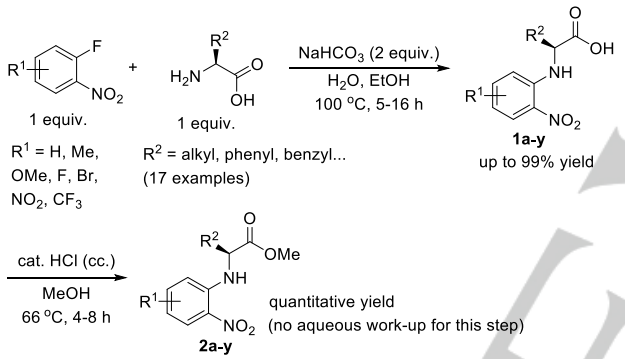
[a] Dazhi Li, and Prof. Dr. Thierry Ollevier
Département de chimie, Université Laval
1045 avenue de la Médecine, Québec, QC, G1V 0A6, Canada
E-mail: thierry.ollevier@chm.ulaval.ca
Homepage: https://www.chm.ulaval.ca/tollevier/

Supporting information for this article is given via a link at the end of the document.

Results and Discussion

o-Nitrofluorobenzene was first reacted with various amino acids in a H_2O/EtOH mixture as solvent (Scheme 2). Although microwave-assisted conditions have been reported to provide shorter reaction times,[13] conventional heating was chosen because, under microwave-assisted conditions, the product was racemized to some extent.[8h, 8r] The yields of **1** were usually high (> 90%).[14]

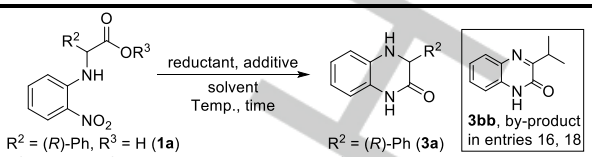
In the next step, (*o*-nitrophenyl)-amino acids from *L*-valine and (*R*)-phenylglycine were selected firstly in the optimization study of the preparation of **2**. Several esterification methods have been reported: using $SOCl_2$,[15] CH_3I[8l] or $(CH_3)_2SO_4$.[8k] At first, stoichiometric $SOCl_2$ was used and 90% isolated yield was obtained for both **2a** and **2b**. Considering the acid waste generated by using stoichiometric $SOCl_2$ and trace pollutants of sulfur which could poison some metal catalyst,[16] $SOCl_2$ was replaced with catalytic HCl (10 mol%, 12 M in water). By heating **1** in methanol with HCl, esters **2** were successfully obtained. The use of catalytic HCl required no aqueous work-up and almost quantitative yields of the esters were obtained for all cases.



Scheme 2. Synthesis of *N*-(*o*-nitroaryl) amino acid esters.

In the last step, different conditions were tested for the reductive cyclization of dihydroquinoxalinones. First, Zn and Fe were used in H_2O/EtOAc (Table 1, Entries 1–8). The reaction of acid **1a** and Zn gave 36% yield (Entry 1). A faster reaction was observed with ester **2a** and a better yield (58%) was obtained with less Zn (Entry 2). The best result (93% yield, 99.2% *ee*) was obtained with Fe instead of Zn, although the reaction needed a longer time (Entry 3). Substrates **1b** and **2b** from *L*-valine shared a similar trend (Entries 4–8). According to the stoichiometry of the reaction, the reduction of $–NO_2$ to $–NH_2$ requires 3 equiv. of Fe, where only a moderate yield of **3b** (70%) was obtained (Entry 6). A full conversion was only obtained when 6 equiv. of Fe were used (Entry 8 *vs.* 7 and 6). Iron was believed to be partially poisoned with reaction conditions comprising an air-saturated solution. In addition to Zn and Fe, Mg and Al were tested as well (Entries 9–10), but most of **2b** remained unreacted. The reaction using $NaBH_4/BiCl_3$[17] was fast and 77% yield was obtained (Entry 11). Using $Fe/CaCl_2$ in H_2O/EtOH[18] gave 78% yield (Entry 12) and changing the solvent to H_2O/EtOAc gave a slightly better 84% yield (Entry 13). Recently iron-catalyzed reductive cyclization of *o*-nitrostyrenes into indoles using a silane as terminal reductant has been reported.[19] However, such catalytic conditions have not been applied in the reductive cyclization of *N*-(*o*-nitroaryl)-amino esters into dihydro-quinoxalinones. Thus, the conditions using silanes and catalytic $Fe(OAc)_2$ were tested (Entries 14–19). Without any ligand, $PhSiH_3$ with $Fe(OAc)_2$ gave less than 9% yield (Entry 14). With 1,10-phenanthroline (**L1**) as ligand, the reaction gave 71% yield (Entry 15). Changing the $PhSiH_3$ to Ph_2SiH_2, the yield dropped to 11% (Entry 16) and 32% of by-product **3bb** was also isolated. Using $PhMe_2SiH$, no conversion was observed (Entry 17). Using polymethylhydrosiloxane

Table 1. Optimization of the reaction conditions.



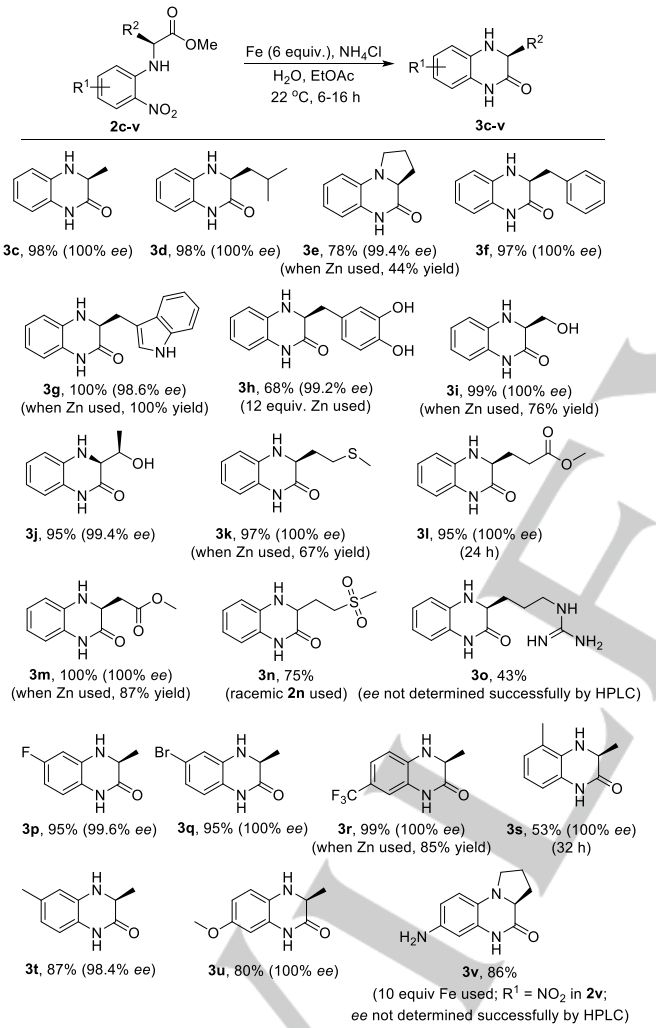
R^2 = (*R*)-Ph, R^3 = H (**1a**)
R^2 = (*S*)-*i*Pr, R^3 = H (**1b**)
R^2 = (*R*)-Ph, R^3 = Me (**2a**)
R^2 = (*S*)-*i*Pr, R^3 = Me (**2b**)

R^2 = (*R*)-Ph (**3a**)
R^2 = (*S*)-*i*Pr (**3b**)

Entry	**1** or **2**	Reductant (equiv.)/Additive	T (°C)	t (h)	Yield (%)[h]
1[a]	**1a**	Zn (10)/NH_4Cl	22	2	36
2[a]	**2a**	Zn (5)/NH_4Cl	22	0.5	58
3[a]	**2a**	Fe (8)/NH_4Cl	22	16	93
4[a]	**1b**	Zn (10)/NH_4Cl	22	2	27
5[a]	**2b**	Zn (5)/NH_4Cl	22	2	98
6[a]	**2b**	Fe (3)/NH_4Cl	22	16	70
7[a]	**2b**	Fe (5)/NH_4Cl	22	16	88
8[a]	**2b**	Fe (6)/NH_4Cl	22	8	96
9[a]	**2b**	Mg (6)/NH_4Cl	80	24	<5[i]
10[a]	**2b**	Al (6)/NH_4Cl	80	24	<1[i]
11[b]	**2b**	$NaBH_4$ (8)/$BiCl_3$	22	0.2	77
12[c]	**2b**	Fe (3)/$CaCl_2$	80	24	78
13[d]	**2b**	Fe (3)/$CaCl_2$	80	24	84
14[e]	**2b**	$PhSiH_3$ (3)/$Fe(OAc)_2$	80	48	<9[i]
15[e, f]	**2b**	$PhSiH_3$ (3)/$Fe(OAc)_2$	80	48	71
16[e, f]	**2b**	Ph_2SiH_2 (3)/$Fe(OAc)_2$	80	48	11[j]
17[e, f]	**2b**	$PhMe_2SiH$ (3)/$Fe(OAc)_2$	80	48	NR[k]
18[e, f]	**2b**	PMHS (15)/$Fe(OAc)_2$	80	48	24[l]
19[e, g]	**2b**	$PhSiH_3$ (3)/$Fe(OAc)_2$	80	48	27

Reaction conditions: [a] acid **1** or ester **2** (0.8 mmol), reductant, NH_4Cl (10 mmol), H_2O/EtOAc (6 mL/6 mL). [b] **2** (0.8 mmol), $NaBH_4$, $BiCl_3$ (1.2 mmol), EtOH (5 mL). [c] **2** (0.8 mmol), Fe, $CaCl_2$ (0.8 mmol), H_2O/EtOH (0.2 mL/2 mL). [d] Using H_2O/EtOAc (1 mL/1 mL) as solvent compared to entry 11. [e] **2** (0.8 mmol), reductant, $Fe(OAc)_2$ (10 mol%), 1,2-dimethoxyethane (2 mL). [f] ^{f}1,10-phenanthroline (**L1**, 10 mol%) was added as ligand. [g] [2,2'-bipyridine]-6,6'-diyldimethanol (**L2**, 10 mol%) was added as ligand. [h] Isolated yield. [i] Yield estimated by ^{1}H NMR; most of **2b** remained. [j] 32% of **3bb** also isolated. [k] NR = no reaction. [l] 44% of **3bb** was also isolated.

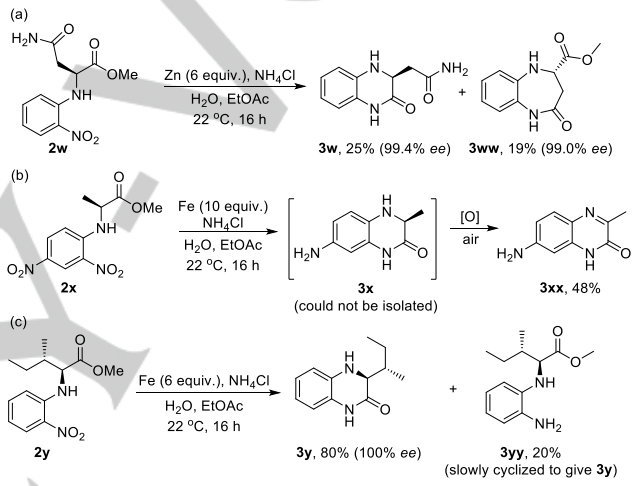
(PMHS), 24% yield was obtained (Entry 18). With ligand **L2** ([2,2'-bipyridine]-6,6'-diyldimethanol) and $PhSiH_3$, the reaction afforded 27% yield (Entry 19). In addition to the conditions above, many other known conditions to reduce aromatic nitro groups were tested as well. By using $Bi/(NH_4)_2SO_4$[20] or $Fe/Zn/BiCl_3$[21] no conversion was obtained. When Zn/Mg/hydrazine[22] were used, most esters were hydrazinolyzed. In the case of **3b**, the use of Zn (Entry 5) gave better yield than Fe (Entry 7; 100% *ee*), but for the most of other cases (**3a**, **3e**, **3i**, **3k**, **3m** and **3r**, Table 1 and Scheme 3) the use of Zn resulted in less clean reactions and gave lower yields than Fe. Thus, the conditions using Fe/NH_4Cl were selected for the reaction scope since they provided the best yields of cyclized products at room temperature.



Scheme 3. Reductive cyclization reaction into of 3,4-dihydroquinoxalin-2(1*H*)-ones–Scope. [a, b]

[a] Reaction conditions: **2** (0.8 mmol), Fe (6.0 equiv; other cases are specifically indicated), saturated aqueous solution of NH_4Cl (6 mL), EtOAc (6 mL). [b] Isolated yields; *ee* was determined by chiral HPLC.

As shown in Scheme 3, most of substrates underwent the reductive cyclization to give the corresponding chiral dihydroquinoxalinones in good to excellent yields under mild conditions. In addition to phenyl (**3a**), alkyl (**3b**–**e**), benzyl (**3f**, **3g**), alkoxy (**3i**, **3j**), sulfide (**3k**) and ester (**3l**, **3m**) substituted groups, this study expanded the substrate scope to dihydroxybenzyl (**3h**), sulfone (**3n**), guanidyl (**3o**) and amide (**3w**) groups (Schemes 3 and 4a). In addition to the unsubstituted substrates on the benzene ring of dihydroquinoxalinones, other substituted substrates were studied. Seven substituents were chosen, including electron-withdrawing (**3p**–**r**) and electron-donating (**3s**–**v**) groups. Starting with substrates possessing electron-withdrawing groups, the yields were 95–99%, whereas, with electron-donating groups, the yields were 48–87%. For the synthesis of **3h** (Scheme 3) and **3w** (Scheme 4a), Fe was not an efficient reductant and the reason remained unclear. However, **3h** and **3w** were obtained by using Zn instead.

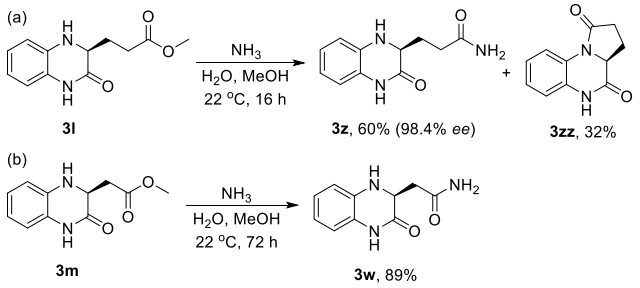


Scheme 4. Synthesis of 3,4-dihydroquinoxalin-2(1*H*)-ones **3w**, **3x**, and **3y**.

The obtention of **3w** and **3ww** (Scheme 4a) showed that the cyclization happened both at the amide and the ester group of *L*-asparagine. During the synthesis of **3u** (Scheme 3), it was found that **3u** was air-oxidized slowly in an EtOAc solution to give the corresponding quinoxalinone. The oxidation of **3x** (with a $–NH_2$ at C7 position, Scheme 4b) was even faster compared to **3u** (see Supporting Information Figure S1 and S2). According to Krchňák,[8h] **3c** was air-oxidized in AcOH solution. The oxidation cases of **3u** and **3x** are thus consistent with this previous report. The observation of the easy oxidation of **3u** and **3x** explained the reason why dihydroquinoxalinones with an electron-donating group on the benzene ring were rarely met in the literature. Using mild conditions, these two molecules could be obtained (**3u** and crude **3x** were stable as solids). The oxidation problem was solved by using substrates with a substituent at the N4 position, such as **3v**. During the synthesis of **3y**, the non-cyclized by-product **3yy** was isolated in a 20% yield (Scheme 4c). It was found that **3yy** did not cyclize completely after 19 days, as monitored by ^1H NMR (see Supporting Information Figure S3).

Starting from *L*-glutamine, **3z** (Scheme 5a) could not be obtained due to the hydrolysis of the amide group under the optimized conditions. Fortunately, **3z** (60%) and a by-product **3zz** (32%) were obtained by the ammonolysis of **3l**. Because the

reductive cyclization towards **3w** gave a low yield (Scheme 4a), the ammonolysis method is also valuable and **3w** was obtained in 89% yield (Scheme 5b).



Scheme 5. Ammonolysis of substrates **3l** and **3m**.

In this study, the enantiopurity of the obtained products was a major aspect to address. The enantiopurities of 23 final products were determined by chiral HPLC and were found in the range of 98.4–100% *ee*. Furthermore, each step of the synthesis of **3l** was studied in extended reaction times.[23] In all steps, the enantiopurity of (*S*)-**3l** remained intact. This further proves that the whole synthetic procedure to obtain enantiopure dihydroquinoxalinones was reliable.

Conclusions

In conclusion, a general and efficient synthetic approach was developed for the efficient synthesis of enantiopure dihydroquinoxalinones. It involves a reductive cyclization using cheap and non-toxic Fe under mild conditions in water and ethyl acetate. The scope of reaction appeared to be general and various functional groups were tolerated. Dihydroquinoxalinones with electron-donating groups on the benzene ring were found air-oxidized in solution. Moreover, the enantiopurity of the dihydroquinoxalinones was determined by chiral HPLC and it was demonstrated that no racemization occurs during the process. Other studies involving Fe as a mediator in reductive cyclization transformations are in progress. Further developments will be reported in due course.

Experimental Section

General information: All experiments were run under air without using an inert atmosphere. All materials are commercially available and were used as received without further purification. Thin-layer chromatography (TLC) was performed on commercial silica gel plates (250 µm; Silicycle F254) and compounds were visualized using UV light. The compounds were purified on silica gel column (200–300 mesh) unless stated otherwise. IR spectra were measured on a Bomem Michelson 100 Series FTIR spectrometer using NaCl window. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Varian Inova 400 MHz or Agilent Technologies DD2 500 MHz spectrometers. Chemical shifts are given in ppm and residual solvent peaks were used as reference. The coupling constants were reported in hertz. High-resolution mass spectra (HRMS) were recorded on a LC/MS-TOF Agilent 6210 mass spectrometer (electrospray ionization). Melting points are uncorrected and were recorded on a MEL-TEMP® capillary melting point apparatus. Optical rotations were measured on a Jasco DIP-360 digital polarimeter using sodium lamp at room temperature. Enantiopurities were determined on an Agilent 1100 Series HPLC system using Daicel ChiralCel® OJ–H, OD–H, and AD–H columns.

Typical procedure of the synthesis of 3,4-dihydro-quinoxalin-2(1*H*)-ones 3: To a stirred solution of *N*-(*o*-nitroaryl) amino acid methyl esters **2** (0.8 mmol, 1.0 equiv.) in EtOAc (6 mL) was added a saturated aqueous NH_4Cl solution (6 mL), followed by the addition of Fe or Zn powder (4.8 mmol, 6.0 equiv.). The yellow-gray mixture was stirred strongly (1000 r/min) at 20–25 °C for 2–16 h and finally it became a black mixture (For zinc, the mixture finally became a white-gray mixture from yellow-gray suspension). After completion of reaction monitored by TLC, the mixture was diluted with EtOAc (30 mL) and filtered through filter paper. The filtrate was extracted with ethyl acetate (2×10 mL). The organic solution was dried over Na_2SO_4 and concentrated to give a brown crude product, which was purified on silica gel column chromatography using hexane/EtOAc or CH_2Cl_2/MeOH as eluent to give the dihydroquinoxalinones (25–100% yield). The characterization data for each compound is shown below.

(*R*)-3-Phenyl-3,4-dihydroquinoxalin-2(1*H*)-one (3a):[8f] 0.166 g, 93% yield, 99.2% *ee*. White solid; m.p. 147–148 °C. R_f = 0.60 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = –94.8 (c = 0.25, MeOH). IR: $\tilde{\nu}$ = 3322, 3204, 3063, 2964, 1677, 1604, 1507, 1376, 741, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.50 (s, 1H), 7.47–7.38 (m, 2H), 7.37–7.27 (m, 3H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.79–6.64 (m, 3H), 5.08 (s, 1H), 4.29 (s, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.52, 139.14, 132.89, 128.81, 128.45, 127.19, 124.70, 124.10, 119.30, 115.82, 113.65, 60.61 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{14}H_{12}N_2O+H]^+$ $[M+H]^+$ 225.1022, found 225.1027. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 0.5 mL/min, detected wavelength: 240 nm, retention time: 36.26 min ((*R*)-enantiomer), 41.11 min ((*S*)-enantiomer) (lit.,[8g] 35.7 min ((*R*)-enantiomer); 38.3 min ((*S*)-enantiomer)).

(*S*)-3-Isopropyl-3,4-dihydroquinoxalin-2(1*H*)-one (3b):[8b] 0.145 g, 96% yield, 100% *ee*. White solid; m.p. 84–85 °C. R_f = 0.62 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +24.1 (c 0.6, $CHCl_3$) (lit.,[8b] $[\alpha]_D^{22}$ = +21.1 (c = 0.6, $CHCl_3$)). $[\alpha]_D^{20}$ = +46.9 (c 0.25, MeOH). IR: $\tilde{\nu}$ = 3343, 3208, 3066, 2962, 2932, 2873, 1674, 1605, 1507, 1377, 1297, 1253, 741 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.91 (s, 1H), 6.93–6.80 (m, 1H), 6.73–6.53 (m, 3H), 4.01 (s, 1H), 3.77 (d, *J* = 5.3 Hz), 2.34–2.14 (m, 1H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.82, 133.31, 124.92, 123.84, 118.70, 115.49, 113.35, 61.73, 30.87, 19.02, 17.51 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{11}H_{14}N_2O+H]^+$ $[M+H]^+$ 191.1179, found 191.1178. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 6.935 min ((*S*)-enantiomer); Chiralcel® OD–H column (4.6 mm×250 mm), hexane:*i*PrOH = 99:1, flow rate: 0.5 mL/min, detected wavelength: 230 nm, retention time: 54.77 min ((*S*)-enantiomer) (lit.,[7a] 57.70 min ((*S*)-enantiomer); 65.83 min ((*R*)-enantiomer)).

(*S*)-3-Methyl-3,4-dihydroquinoxalin-2(1*H*)-one (3c):[8b] 0.128 g, 98% yield, 100% *ee*. White solid; m.p. 111–113 °C. R_f = 0.37 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +95.0 (c = 0.25, MeOH). IR: $\tilde{\nu}$ = 3320, 3216, 3064, 2975, 1678, 1606, 1506, 1376, 1311, 745 cm^{-1}. ^{1}H NMR (400 MHz, CDCl3) δ = 8.64 (s, 1H), 6.95–6.84 (m, 1H), 6.80–6.72 (m, 2H), 6.68 (d, *J* = 7.8 Hz, 1H), 4.02 (q, *J* = 6.7 Hz, 1H), 3.85 (s, 1H), 1.47 (d, *J* = 6.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.47, 133.44, 125.62, 123.77, 119.59, 115.40, 114.09, 51.94, 17.88 ppm. HRMS (ESI-TOF): m/z calcd for $[C_9H_{10}N_2O+H]^+$ $[M+H]^+$ 163.0866, found 163.0866. Chiral HPLC conditions: Chiralcel® AD–H column (4.6 mm×250 mm), hexane/*i*PrOH = 70:30, flow rate: 1 mL/min, detected wavelength: 254 nm, retention time: 6.02 min ((*S*)-enantiomer).

(*S*)-3-Isobutyl-3,4-dihydroquinoxalin-2(1*H*)-one (3d):[8b] 0.161 g, 98% yield, 100% *ee*. Yellow viscous oil. R_f = 0.75 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +47.2 (c = 0.75, MeOH). IR: $\tilde{\nu}$ = 3333, 3211, 3066, 2956, 2870, 1677, 1605, 1507, 1377, 1303, 744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.68 (s, 1H), 6.99–6.86 (m, 1H), 6.80–6.72 (m, 2H), 6.68 (d, *J* = 7.8 Hz, 1H), 3.93–3.97 (m, 2H), 1.83–1.59 (m, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.96 (d, *J* = 6.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.40, 132.82, 125.43, 123.80, 119.44, 115.34, 114.26, 54.55, 40.16, 24.25, 23.29, 21.46 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{12}H_{16}N_2O+H]^+$ $[M+H]^+$ 205.1335, found 205.1334. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 6.35 min ((*S*)-enantiomer).

(*S*)-1,2,3,3a-Tetrahydropyrrolo[1,2-*a*]quinoxalin-4(5*H*)-one (3e):[8b] 0.116 g, 78% yield, 99.4% *ee*; Light yellow solid; m.p. 164–165 °C. R_f = 0.55 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = –94.0 (c = 0.25, MeOH); IR: $\tilde{\nu}$ = 3198, 3075, 2979, 2927, 1679, 1612, 1509, 1405, 1365, 1321, 741 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.82 (s, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 1H), 3.73 (dd, *J* = 9.0, 7.0 Hz, 1H), 3.49 (td, *J* = 8.6, 5.2 Hz, 1H), 3.19 (td, *J* = 9.2, 6.0 Hz, 1H), 2.37–2.27 (m, 1H), 2.22–1.98 (m, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.71, 135.16, 126.86, 123.98, 118.46, 115.12, 111.96, 60.07, 46.42, 26.75, 22.20 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{11}H_{12}N_2O+H]^+$ $[M+H]^+$ 189.1022, found 189.1022. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 0.5 mL/min, detected wavelength: 240 nm, retention time: 17.51 min ((*S*)-enantiomer), 19.68 min ((*R*)-enantiomer).

(*S*)-3-Benzyl-3,4-dihydroquinoxalin-2(1*H*)-one (3f):[8b] 0.186 g, 97% yield, 100% *ee*; Light yellow solid; m.p. 189–190 °C. R_f = 0.67 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = -45.34 (c = 0.5, $CHCl_3$) (lit.,[8b] $[\alpha]_D^{22}$ = -45.90 (c = 0.5, $CHCl_3$)). $[\alpha]_D^{20}$ = -57.6 (c = 0.18, MeOH). IR: $\tilde{\nu}$ = 3371, 3208, 3062, 2961, 2923, 1680, 1604, 1506, 1376, 1307, 745, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.88 (s, 1H), 7.43–7.27 (m, 3H), 7.22 (d, *J* = 7.5 Hz, 2H), 6.97–6.87 (m, 1H), 6.85–6.73 (m, 2H), 6.59 (d, *J* = 7.6 Hz, 1H), 4.15–4.01 (m, 1H), 3.86 (s, 1H), 3.27 (dd, *J* = 13.0, 2.7 Hz, 1H), 2.86 (dd, *J* = 13.0, 11.8 Hz, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 168.66, 136.82, 132.41, 129.40 (d, J_{NC} = 13.3 Hz), 128.96 (d, J_{NC} = 11.2 Hz), 127.10, 125.38, 124.07, 119.58, 115.48, 114.61, 57.82 (d, J_{NC} = 10.5 Hz), 37.52 (d, J_{NC} = 6.7 Hz) ppm. HRMS (ESI-TOF): m/z calcd for $[C_{15}H_{14}N_2O+H]^+$ $[M+H]^+$ 239.1179, found 239.1178. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 9.162 min ((*S*)-enantiomer);[8g] Chiralcel® OD–H column (4.6 mm×250 mm), hexane:*i*PrOH = 85:15, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 11.78 min ((*S*)-enantiomer) (lit.,[7a] 17.717 min ((*S*)-enantiomer), 26.785 ((*R*)-enantiomer)).

(*S*)-3-((1H-Indol-3-yl)methyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3g):[8b] 0.167 g, 100% yield, 99.6% *ee* (0.60 mmol of **2g** used); Yellow solid; m.p. 89–90 °C. R_f = 0.34 (hexane/EtOAc = 1:1, v/v); $[\alpha]_D^{20}$ = +3.0 (c = 0.25, MeOH). IR: $\tilde{\nu}$ = 3366, 3056, 2957, 2927, 1674, 1604, 1506, 1422, 1376, 1307, 1234, 1119, 741 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.80 (s, 1H), 8.23 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 8.0,1H), 7.15 (t, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 1.8 Hz, 1H), 6.92–6.84 (m, 1H), 6.83–6.72 (m, 2H), 6.52 (d, *J* = 7.7 Hz, 1H), 4.18 (dd, *J* = 11.2, 2.7 Hz, 1H), 3.98 (s, 1H), 3.48 (dd, *J* = 14.4, 2.7 Hz, 1H), 3.07 (dd, *J* = 14.4, 11.2 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.03, 136.45, 132.70, 127.17, 125.34, 123.92, 123.30, 122.50, 119.80, 119.35, 118.87, 115.38, 114.55, 111.35, 110.84, 56.71, 27.60 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{17}H_{15}N_3O+H]^+$ $[M+H]^+$ 278.1288, found 278.1287. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 0.5 mL/min, detected wavelength: 240 nm, retention time: 9.74 min ((*S*)-enantiomer), 11.83 min ((*R*)-enantiomer).

(*S*)-3-(3,4-Dihydroxybenzyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3h):[24] 16.7 mg, 68% yield , 99.2% *ee* (0.090 mmol of **2h** used, 12 equiv. of Zn used). White solid; m.p. 86–90 °C. R_f = 0.44 (CH_2Cl_2/MeOH = 10:1, v/v). $[\alpha]_D^{20}$ = –84.8 (c = 0.07, MeOH). IR: $\tilde{\nu}$ = 3330, 3067, 2960, 2919, 1673, 1604, 1507, 1425, 1367, 1288, 1230, 749 cm^{-1}. ^1H NMR (400 MHz, CD_3COCD_3) δ = 9.31 (s, 1H), 7.85 (s, 2H), 6.88–6.63 (m, 6H), 6.54 (d, *J* = 7.7 Hz, 1H), 5.04 (s, 1H), 3.97–3.86 (m, 1H), 2.96 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.65 (dd, *J* = 13.4, 10.0 Hz, 1H) ppm. ^{13}C NMR (101 MHz, CD_3COCD_3) δ = 167.40, 144.96, 143.71, 133.49, 128.86, 126.34, 122.95, 120.75, 118.34, 116.35, 115.26, 114.67, 114.27, 57.92, 36.88 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{15}H14_4N_2O_3+H]^+$ $[M+H]^+$ 271.1077, found 271.1079. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 20:80, flow rate: 0.5 mL/min, detected wavelength: 240 nm, retention time: 9.02 min ((*R*)-enantiomer), 9.46 min ((*S*)-enantiomer).

(*S*)-3-(Hydroxymethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3i):[8b] 0.141 g, 99% yield, 100% *ee*; White solid; m.p. 123–125 °C. R_f = 0.10 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +34.3 (c = 0.25, MeOH). IR: $\tilde{\nu}$ = 3318, 3069, 2918, 1674, 1606, 1507, 1428, 1383, 1309, 1060, 746 cm^{-1}. ^1H NMR (400 MHz, CD_3SOCD_3) δ = 10.17 (s, 1H), 6.76 – 6.61 (m, 3H), 6.49 (dp, *J* = 7.8, 3.8 Hz, 1H), 5.87 (s, 1H), 4.84 (t, *J* = 5.2 Hz, 1H), 3.75 (dd, *J* = 6.8, 3.1 Hz, 1H), 3.68–3.56 (m, 1H), 3.55–3.44 (m, 1H) ppm. ^{13}C NMR (101 MHz, CD_3SOCD_3) δ = 166.57, 134.39, 125.82, 123.11, 117.62, 114.94, 113.71, 62.34, 58.09 ppm. HRMS (ESI-TOF): m/z calcd for $[C_9H_{10}N_2O_2+H]^+$ $[M+H]^+$ 179.0815, found 179.0815. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 0.5 mL/min, detected wavelength: 240 nm, retention time: 15.89 min ((*S*)-enantiomer).

(*S*)-3-((R)-1-Hydroxyethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3j): 0.149 g, 95% yield, 99.4% *ee*. Yellow solid; m.p. 39–41 °C. R_f = 0.16 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +30.9 (c = 0.60, MeOH); IR: $\tilde{\nu}$ = 3333, 3220, 3065, 2973, 2932, 1673, 1606, 1507, 1425, 1378, 1300, 1075, 919, 741 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.89 (s, 1H), 7.01–6.84 (m, 1H), 6.79–6.62 (m, 3H), 4.21 (s, 1H), 4.16–4.05 (m, 1H), 3.94 (d, *J* = 5.1 Hz, 1H), 2.92 (d, *J* = 6.1 Hz, 1H), 1.36 (d, *J* = 6.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 167.55, 132.70, 124.51, 124.18, 119.39, 115.46, 114.20, 67.71, 61.05, 19.32 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{10}H_{12}N_2O_2+H]^+$ $[M+H]^+$ 193.0972, found 193.0974. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 6.77 min ((*S*)-enantiomer), 9.66 min ((*R*)-enantiomer).

(*S*)-3-(2-(Methylthio)ethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3k):[8m] 0.173 g, 97% yield, 100% *ee*. Yellow viscous oil. R_f = 0.51 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +34.2 (c = 0.71, MeOH). IR: $\tilde{\nu}$ = 3326, 3213, 3066, 2965, 2915, 1677, 1605, 1507, 1426, 1376, 1309, 745 cm^{-1}. ^1H NMR (400 MHz, CDCl3) δ = 8.97 (s, 1H), 6.95–6.84 (m, 1H), 6.79–6.72 (m, 2H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.26 (s, 1H), 4.16–4.05 (m, 1H), 2.81–2.56 (m, 2H), 2.24–2.13 (m, 1H), 2.13 (s, 3H), 2.09–1.97 (m, 1H) ppm. ^{13}C NMR (101 MHz, CDCl3) δ = 168.73, 132.85, 125.25, 123.95, 119.53, 115.46, 114.27, 55.66 (d, J_{NC} = 4.9 Hz), 30.39, 30.35, 15.35 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{11}H_{14}N_2OS+H]^+$ $[M+H]^+$ 223.0900, found 223.0900. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 11.65 min ((*S*)-enantiomer).

Methyl (*S*)-3-(3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)-propanoate (3l): 0.179 g, 95% yield, 100% *ee*. Light yellow solid; m.p. 73–74 °C. R_f = 0.39 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +42.8 (c = 0.25, MeOH). IR: $\tilde{\nu}$ = 3334, 3067, 2952, 1723, 1678, 1606, 1507, 1436, 1375, 1307, 746 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 9.09 (s, 1H), 6.93–6.85 (m, 1H), 6.78–6.71 (m, 2H), 6.67 (d, *J* = 7.9 Hz, 1H), 4.16 (s, 1H), 4.02 (t, *J* = 5.6 Hz, 1H), 3.67 (s, 3H), 2.66–2.45 (m, 2H), 2.30–2.09 (m, 2H) ppm. ^{13}C NMR

(101 MHz, $CDCl_3$) δ = 174.01, 168.34, 133.09, 125.16, 123.91, 119.45, 115.44, 114.16, 55.55, 51.83 (d, J_{NC} = 4.1 Hz), 29.92, 26.83 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{12}H_{14}N_2O_3+H]^+$ $[M+H]^+$ 235.1077, found 235.1079. Chiral HPLC conditions: Chiralcel® AD–H column (4.6 mm×250 mm), hexane/*i*PrOH = 70:30, flow rate: 1 mL/min, detected wavelength: 254 nm, retention time: 7.70 min ((*S*)-enantiomer).

Methyl (*S*)-2-(3-oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)acetate (3m):[8m] 0.177 g, 100% yield, 100% *ee*. White solid; m.p. = 83–84 °C. R_f = 0.54 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = –21.7 (c = 0.25, MeOH). IR: ṽ = 3330, 3212, 3067, 2953, 1728, 1683, 1606, 1508, 1434, 1365, 1309, 1176, 746 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.93 (s, 1H), 6.95–6.86 (m, 1H), 6.81–6.73 (m, 2H), 6.70 (d, *J* = 7.9 Hz, 1H), 4.73 (s, 1H), 4.35 (dt, *J* = 10.4, 2.0 Hz, 1H), 3.75 (s, 3H), 3.14 (dd, *J* = 17.3, 2.0 Hz, 1H), 2.75 (dd, *J* = 17.3, 10.4 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 172.32, 167.42, 132.85, 125.00, 124.08, 119.67, 115.47, 114.44, 52.83, 52.08, 35.82 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{11}H_{12}N_2O_3+H]^+$ $[M+H]^+$ 221.0921, found 221.0920. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 60:40, flow rate: 0.5 mL/min, detected wavelength: 240 nm, retention time: 20.07 min ((*S*)-enantiomer).

3-(2-(Methylsulfonyl)ethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3n): 0.114 g (racemic starting material used), 75% yield (0.60 mmol of racemic **2n** used). Yellow solid; m.p. 174–179 °C. R_f = 0.38 (CH_2Cl_2/MeOH = 10:1, v/v). IR: ṽ = 3343, 3067, 3013, 2927, 1681, 1608, 1508, 1377, 1303, 1132, 750 cm^{-1}. ^1H NMR (500 MHz, CD_3SOCD_3) δ = 10.35 (s, 1H), 6.78 (t, J = 7.6 Hz, 1H), 6.73 (d, J = 7.6 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 6.61 (t, *J* = 7.6 Hz, 1H), 6.15 (s, 1H), 3.91 (t, *J* = 5.3 Hz, 1H), 3.32–3.18 (m, 2H), 2.99 (s, 3H), 2.15–1.96 (m, 2H) ppm. ^{13}C NMR (101 MHz, CD_3SOCD_3) δ = 166.69, 133.77, 125.74, 122.94, 118.09, 114.83, 113.69, 53.81, 50.09, 40.22, 24.16 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{11}H_{14}N_2O_3S+H]^+$ $[M+H]^+$ 225.0798, found 225.0796.

(*S*)-1-(3-(3-Oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)propyl)-guanidine (3o): 85.1 mg, 43% yield. Yellow viscous oil. R_f = 0.07 (CH_2Cl_2/MeOH = 10:1, v/v). $[\alpha]_D^{20}$ = +42.2 (c = 0.32, MeOH). IR: ṽ = 3332, 3168, 2962, 1667, 1651, 1506, 1424, 1379, 1310, 749 cm^{-1}. ^1H NMR (400 MHz, D_2O) δ = 7.03–6.95 (m, 1H), 6.93–6.76 (m, 3H), 3.88 (t, *J* = 5.6 Hz, 1H), 3.14 (t, *J* = 6.0 Hz, 2H), 1.77–1.60 (m, 4H) ppm. ^{13}C NMR (101 MHz, D_2O) δ = 171.48, 157.26, 133.43, 125.80, 125.36, 120.80, 116.49, 115.71, 55.90, 41.33, 28.48, 24.37 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{12}H_{17}N_5O+H]^+$ $[M+H]^+$ 248.1506, found 248.1507. *ee* was not determined successfully using HPLC.

(*S*)-6-Fluoro-3-methyl-3,4-dihydroquinoxalin-2(1*H*)-one (3p):[8m] 0.424 g, 95% yield, 99.6 % *ee* (2.48 mmol of **2p** used). Brown solid; m.p. = 110–112 °C. R_f = 0.46 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +72.2 (c = 0.17, MeOH); IR: ṽ = 3320, 3225, 3087, 2977, 2934, 1681, 1629, 1520, 1449, 1371, 1310, 1167, 838, 795 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 9.43 (s, 1H), 6.71 (dd, *J* = 8.5, 5.2 Hz, 1H), 6.53–6.31 (m, 2H), 4.02 (q, *J* = 6.7 Hz, 1H), 3.97 (s, 1H), 1.46 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.29, 159.46 (d, J_{FC} = 240.4 Hz), 134.53 (d, J_{FC} = 10.7 Hz), 121.69 (d, J_{FC}= 2.3 Hz), 116.13 (d, J_{FC}= 9.8 Hz), 105.51 (d, J_{FC} = 23.2 Hz), 101.26 (d, J_{FC} = 26.6 Hz), 51.57, 18.04 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = –118.97 (td, J_{FH} = 9.0, 5.2 Hz) ppm. HRMS (ESI-TOF): m/z calcd for $[C_9H_9FN_2O+H]^+$ 1$[M+H]^+$ 81.0772, found 181.0772. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 8.60 min ((*S*)-enantiomer), 10.83 min ((*R*)-enantiomer).

(*S*)-6-Bromo-3-methyl-3,4-dihydroquinoxalin-2(1*H*)-one (3q):[8p] 0.138 g, 95% yield, 100% *ee* (0.60 mmol of **2q** used); White solid; m.p. 132–134 °C. R_f = 0.49 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +74.4 (c = 0.25, MeOH); IR: ṽ = 3381, 3205, 3070, 2969, 2921, 1683, 1611, 1505, 1400, 1359, 1307, 795 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 9.38 (s, 1H), 6.85 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.80 (d, *J* = 1.9 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 4.02 (qd, *J* = 6.7, 1.4 Hz, 1H), 3.92 (s, 1H), 1.45 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.45, 134.60, 124.63, 122.09, 116.71, 116.65, 116.04, 51.67, 18.09 ppm. HRMS (ESI-TOF): m/z calcd for $[C_9H_9BrN_2O+H]^+$ $[M+H]^+$ 240.9971 (100%), 242.9951 (97%), found 240.9966 (100%), 242.9946 (97%). Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 11.69 min ((*S*)-enantiomer).

(*S*)-3-Methyl-7-(trifluoromethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3r):[8n] 0.159 g, 99% yield, 100% *ee* (0.70 mmol of **2r** used); White solid; m.p. 149–150 °C. R_f = 0.51 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +41.0 (c 0.25, MeOH). IR: ṽ = 3331, 3222, 3128, 2987, 2881, 1682, 1627, 1514, 1380, 1330,1170, 1111, 892, 812, 713, 647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 9.30 (s, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 7.02 (s, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 4.16 (s, 1H), 4.13 (q, *J* = 6.8 Hz, 1H), 1.51 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.17, 136.12, 125.18, 124.32 (q, J_{FC} = 270.9 Hz), 121.28 (q, J_{FC} = 34.0 Hz), 121.12 (q, J_{FC} = 3.8 Hz), 113.36, 112.48 (q, J_{FC} = 3.8 Hz), 51.65, 18.36 ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ = –61.34 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{10}H_{10}F_3N_2O+H]^+$ $[M+H]^+$ 231.0740, found 231.0740. Chiral HPLC conditions: Chiralcel® AD–H column (4.6 mm×250 mm), hexane/*i*PrOH = 80: 20, flow rate: 1 mL/min, detected wavelength: 254 nm, retention time: 5.54 min ((*S*)-enantiomer).

(*S*)-3,5-Dimethyl-3,4-dihydroquinoxalin-2(1*H*)-one (3s):[8g] 74.7 mg, 53% yield, 100% *ee* (7.5 equiv of Fe used). White solid; m.p. 113–114 °C. R_f = 0.42 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +93.8 (c = 0.17, MeOH). IR: ṽ = 3356, 3207, 3055, 2980, 2938, 1681, 1600, 1488, 1444, 1376, 1312, 767, 734 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.80 (s, 1H), 6.79 (d, *J* = 7.2 Hz, 1H), 6.74–6.60 (m, 2H), 4.06 (q, *J* = 6.7 Hz, 1H), 3.72 (s, 1H), 2.18 (s, 3H), 1.49 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.44, 131.49, 125.26, 125.16, 121.91, 118.95, 113.54, 51.87, 18.19, 16.68 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{10}H_{12}N_2O+H]^+$ $[M+H]^+$ 177.1022, found 177.1023. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), conditions A: hexane/*i*PrOH = 75:25, flow rate: 0.5 mL/min, detected wavelength: 230 nm, retention time: 17.404 min ((*S*)-enantiomer); conditions B: hexane/*i*PrOH = 95:5, flow rate: 0.5 mL/min, retention time: 56.95 min ((*S*)-enantiomer) (lit.,[8g] 54.6 min ((*S*)-enantiomer), 74.2 min ((*R*)-enantiomer).

(*S*)-3,6-Dimethyl-3,4-dihydroquinoxalin-2(1*H*)-one (3t):[8ab] 0.123 g, 87% yield, 98.4% *ee*. White solid; m.p. 128–129 °C. R_f = 0.46 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +102.6 (c = 0.25, MeOH); IR: ṽ = 3326, 3220, 3064, 2975, 2923, 1681, 1620, 1525, 1445, 1361, 1309, 1256, 1135, 802, 737 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 9.08 (s, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 6.56 (d, *J* = 7.9 Hz, 1H), 6.49 (s, 1H), 4.00 (q, *J* = 6.6 Hz, 1H), 3.80 (s, 1H), 2.24 (s, 3H), 1.45 (d, *J* = 6.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.62, 133.50, 133.26, 123.29, 120.10, 115.35, 114.74, 51.96, 20.99, 17.94 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{10}H_{12}N_2O+H]^+$ $[M+H]^+$ 177.1022, found 177.1021. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 8.50 min ((*R*)-enantiomer), 8.83 min ((*S*)-enantiomer).

(*S*)-7-Methoxy-3-methyl-3,4-dihydroquinoxalin-2(1*H*)-one (3u):[25] 76.8 mg, 80% yield, 100% *ee* (0.50 mmol of **2u** used); White solid; m.p. 134–136 °C. R_f = 0.29 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = +96.5 (c = 0.15, MeOH). IR: ṽ = 3340, 3230, 2976, 2934, 1684, 1606, 1520, 1394, 1267, 1242, 1042, 804 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.25 (s, 1H), 6.64 (d, *J* = 8.5 Hz, 1H), 6.47 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.36 (d, *J* = 2.6 Hz, 1H), 3.93 (q, *J* = 6.7 Hz, 1H), 3.75 (s, 3H), 3.61 (s, 1H), 1.44 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.60, 153.83,

127.24, 126.93, 115.20, 108.49, 102.02, 55.78, 52.25, 17.36 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{10}H_{12}N_2O_2+H]^+$ $[M+H]^+$ 193.0972, found 193.0971. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 11.23 min ((*S*)-enantiomer).

(*S*)-7-Amino-1,2,3,3a-tetrahydropyrrolo[1,2-*a*]quinoxalin-4(5*H*)-one (3v):[26] 0.123 g, 86% yield (0.70 mmol of **2v** used; 10 equiv. of Fe used; purified by trituration in ethyl ether). Green-brown solid; m.p. > 200 °C (decomposed). R_f = 0.42 (CH_2Cl_2/MeOH = 10:1, v/v). (Due to the dark color of compound, optical rotation could not be measured successfully); IR: $\tilde{\nu}$ = 3313, 3212, 2953, 2927, 1668, 1623, 1523, 1298, 850, 795 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 8.14 (s, 1H), 6.47 (d, *J* = 8.2 Hz, 1H), 6.37 (d, *J* = 6.7 Hz, 1H), 6.22 (s, 1H), 3.53 (t, *J* = 8.0 Hz, 1H), 3.50 – 3.30 (m, 3H), 3.04 (dd, *J* = 15.8, 8.7 Hz, 1H), 2.32 – 2.13 (m, 2H), 2.12 – 1.89 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.36, 139.24, 128.49, 128.12, 113.59, 110.71, 103.32 (d, J_{NC} = 6.3 Hz), 60.77, 47.17, 26.15, 22.15 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{11}H_{13}N_3O+H]^+$ $[M+H]^+$ 204.1131, found 204.1128. *ee* was not determined successfully using HPLC.

(*S*)-2-(3-Oxo-1,2,3,4-tetrahydroquinoxalin-2-yl)acetamide (3w):[27] 28.9 mg, 25% yield, 99.4% *ee* (0.56 mmol of **2w** used; 6.0 equiv. of Zn used). Yellow solid; m.p. > 260 °C (decomposed). R_f = 0.30 (CH_2Cl_2/MeOH = 10:1, v/v). (Due to the low solubility, the optical rotation was not measured successfully). IR: $\tilde{\nu}$ = 3397, 3346, 3194, 3036, 2921, 1691, 1610, 1509, 1434, 1396, 735 cm^{-1}. ^1H NMR (400 MHz, CD_3SOCD_3) δ = 10.25 (s, 1H), 7.43 (s, 1H), 6.95 (s, 1H), 6.81–6.69 (m, 3H), 6.65–6.55 (m, 1H), 5.84 (s, 1H), 4.12–4.01 (m, 1H), 2.63 (dd, *J* = 16.4, 3.5 Hz, 1H), 2.32 (dd, *J* = 16.4, 8.3 Hz, 1H) ppm. ^{13}C NMR (101 MHz, CD_3SOCD_3) δ = 172.05, 167.53, 134.30, 126.33, 123.15, 118.40, 115.12, 114.27, 53.00, 37.34 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{10}H_{11}N_3O_2+H]^+$ $[M+H]^+$ 206.0924, found 206.0920. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 30:70, flow rate: 1 mL/min, detected wavelength: 240 nm, retention time: 7.41 min ((*R*)-enantiomer), 9.05 min ((*S*)-enantiomer).

Methyl (*S*)-4-oxo-2,3,4,5-tetrahydro-1H-benzo[*b*][1,4]-diazepine-2-carboxylate (3ww): 24.0 mg, 19% yield, 99.0% *ee* (0.56 mmol of **2w** used; 6.0 equiv. of Zn used). Brown solid; m.p. = 82–83 °C. R_f = 0.45 (hexane/EtOAc = 1:1, v/v). $[\alpha]_D^{20}$ = –15.0 (c = 0.11, MeOH). IR: $\tilde{\nu}$ = 3333, 3216, 3066, 2954, 2925, 1728, 1682, 1606, 1508, 1434, 1366, 1309, 1176, 746 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 9.09 (s, 1H, 11-H), 6.93–6.86 (m, 1H, 3-H), 6.79–6.73 (m, 2H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.74 (s, 1H), 4.35 (d, *J* = 10.4 Hz, 1H), 3.74 (s, 3H), 3.14 (dd, *J* = 17.3, 2.5 Hz, 1H), 2.75 (dd, *J* = 17.3, 10.4 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 172.34, 167.54, 132.84, 124.99, 124.11, 119.67, 115.53, 114.44, 52.82, 52.11 (d, J_{NC} = 5.1 Hz), 35.82 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{11}H_{12}N_2O_3+H]^+$ $[M+H]^+$ 221.0921, found 221.0921. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1.0 mL/min, detected wavelength: 240 nm, retention time: 13.04 min ((*S*)-enantiomer), 15.19 min ((*R*)-enantiomer).

7-Amino-3-methylquinoxalin-2(1*H*)-one (3xx):[28] 58.8 mg, 48% yield (0.70 mmol of **2x** used; 10 equiv. of Fe used). Yellow solid; R_f = 0.20 (EtOAc); IR: $\tilde{\nu}$ = 3337, 3224, 2972, 2917, 1667, 1619, 1520, 1370, 1312, 1252, 809 cm^{-1}. ^1H NMR (400 MHz, CD_3SOCD_3) δ = 11.86 (s, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 6.46 (dd, *J* = 8.6, 2.0 Hz, 1H), 6.27 (d, *J* = 2.0 Hz, 1H), 3.40 (s, 2H), 2.22 (s, 3H) ppm. ^{13}C NMR (126 MHz, CD_3SOCD_3) δ = 156.07, 151.06, 150.72, 134.26, 129.15, 124.58, 111.89 (d, J_{NC} = 3.8 Hz), 96.45 (d, J_{NC} = 7.4 Hz), 20.31 (d, J_{NC} = 2.0 Hz) ppm. HRMS (ESI-TOF): m/z calcd for $[C_9H_9N_3O+H]^+$ $[M+H]^+$ 176.0818, found 176.0820.

(*S*)-3-((S)-sec-Butyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3y):[8b] 0.131 g, 80% yield, 100% *ee*. Yellow viscous oil. R_f = 0.72 (hexane/EtOAc = 1:1, v/v); $[\alpha]_D^{20}$ = +54.5 (c = 0.58, MeOH). IR: $\tilde{\nu}$ = 3341, 3210, 3071, 2963, 2930, 2875, 1673, 1605, 1507, 1382, 1310, 1254, 741 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.72 (s, 1H), 6.92–6.82 (m, 1H), 6.75–6.68 (m, 2H), 6.64 (d, J = 7.8 Hz, 1H), 3.98 (s, 1H), 3.84 (d, *J* = 5.2 Hz, 1H), 2.07–1.92 (m, 1H), 1.63–1.52 (m, 1H), 1.33–1.18 (m, 1H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.17, 133.25, 124.80, 123.83, 118.73, 115.17, 113.39, 61.19, 37.41, 24.46, 15.40, 11.46 ppm. HRMS (ESI-TOF): m/z calcd for $[C_{12}H_{16}N_2O+H]^+$ $[M+H]^+$ 205.1335, found 205.1336. Chiral HPLC conditions: Chiralcel® OJ–H column (4.6 mm×250 mm), hexane/*i*PrOH = 75:25, flow rate: 1.0 mL/min, detected wavelength: 240 nm, retention time: 6.70 min ((*S*)-enantiomer).

Acknowledgments

We are grateful to the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Centre in Green Chemistry and Catalysis (CGCC) for financial support of our program. D.L. thanks China Scholarship Council (CSC) for a doctoral scholarship.

Keywords: green chemistry • synthetic methods • iron • zinc • reduction

[1] L. Zhang, R. Qiu, X. Xue, Y. Pan, C. Xu, H. Li, L. Xu, *Adv. Synth. Catal.* **2015**, *357*, 3529-3537.

[2] a) L. M. Cass, K. H. P. Moore, N. S. Dallow, A. E. Jones, J. R. Sisson, W. T. Prince, *J. Clin. Pharmacol.* **2001**, *41*, 528-535; b) J. Ren, C. E. Nichols, P. P. Chamberlain, K. L. Weaver, S. A. Short, J. H. Chan, J.-P. Kleim, D. K. Stammers, *J. Med. Chem.* **2007**, *50*, 2301-2309.

[3] T. P. C. Rooney, P. Filippakopoulos, O. Fedorov, S. Picaud, W. A. Cortopassi, D. A. Hay, S. Martin, A. Tumber, C. M. Rogers, M. Philpott, M. Wang, A. L. Thompson, T. D. Heightman, D. C. Pryde, A. Cook, R. S. Paton, S. Müller, S. Knapp, P. E. Brennan, S. J. Conway, *Angew. Chem., Int. Ed.* **2014**, *53*, 6126-6130; *Angew. Chem.* **2014**, *126*, 6240-6244;

[4] C. T. Eary, Z. S. Jones, R. D. Groneberg, L. E. Burgess, D. A. Mareska, M. D. Drew, J. F. Blake, E. R. Laird, D. Balachari, M. O'Sullivan, A. Allen, V. Marsh, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2608-2613.

[5] D. Catarzi, V. Colotta, F. Varano, O. Lenzi, G. Filacchioni, L. Trincavelli, C. Martini, C. Montopoli, S. Moro, *J. Med. Chem.* **2005**, *48*, 7932-7945.

[6] J. P. Kleim, R. Bender, R. Kirsch, C. Meichsner, A. Paessens, M. Rösner, H. Rübsamen-Waigmann, R. Kaiser, M. Wichers, K. E. Schneweis, *Antimicrob. Agents Chemother.* **1995**, *39*, 2253-2257.

[7] a) Y. Pan, C. Chen, X. Xu, H. Zhao, J. Han, H. Li, L. Xu, Q. Fan, J. Xiao, *Green Chem.* **2018**, *20*, 403-411; b) J.-L. Li, B. Han, K. Jiang, W. Du, Y.-C. Chen, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3952-3954.

[8] a) H. Fu, Y. Jiang, Q. Jiang, D. Jiang, Y. Zhao, *Synlett* **2007**, 1836-1842; b) S. Tanimori, H. Kashiwagi, T. Nishimura, M. Kirihata, *Adv. Synth. Catal.* **2010**, *352*, 2531-2537; c) S. Kamila, E. R. Biehl, *Heterocycles* **2006**, *68*, 1931-1939; d) Y. Sun Park, Y. Min Lee, *Heterocycles* **2009**, *78*, 2233-2244; e) Y. Kim, K. J. Park, Y. S. Choi, M.-S. Lee, Y. S. Park, *Bull. Korean Chem. Soc.* **2013**, *34*, 2531-2534; f) Y. Kim, K. J. Park, Y. S. Park, *Bull. Korean Chem. Soc.* **2012**, *33*, 3853-3856; g) Y. K. Kim, K. H. Kang, E. T. C. Choi, M. H. Lee, Y. S. Park, *Bull. Korean Chem. Soc.* **2007**, *28*, 325-328; h) B. Carbain, E. Schütznerová, A. Přibylka, V. Krchňák, *Adv. Synth. Catal.* **2016**, *358*, 701-706; i) R. E. TenBrink, W. B. Im, V. H. Sethy, A. H. Tang, D. B. Carter, *J. Med. Chem.* **1994**, *37*, 758-768; j) R. J. Holland, I. R. Hardcastle, M. Jarman, *Tetrahedron Lett.* **2002**, *43*, 6435-6437; k) M. J. Donaghy, S. P. Stanforth, *J. Heterocycl. Chem.* **2005**, *42*, 1215-1218; l) D. V. Smil, S. Manku, Y. A. Chantigny, S. Leit, A. Wahhab, T. P. Yan, M. Fournel, C. Maroun, Z. Li, A.-M. Lemieux, A. Nicolescu, J. Rahil, S.

Lefebvre, A. Panetta, J. M. Besterman, R. Déziel, *Bioorg. Med. Chem. Lett.* **2009,** *19*, 688-692; m) B. Xu, Y. Sun, Y. Guo, Y. Cao, T. Yu, *Bioorg. Med. Chem*. **2009**, *17*, 2767-2774; n) C. Neagoie, V. Krchňák, *ACS Comb. Sci*. **2012**, *14*, 399-402; o) Y. Wang, J.-Y. Wach, P. Sheehan, C. Zhong, C. Zhan, R. Harris, S. C. Almo, J. Bishop, S. J. Haggarty, A. Ramek, K. N. Berry, C. O'Herin, A. N. Koehler, A. W. Hung, D. W. Young, *ACS Med. Chem. Lett.* **2016**, *7*, 852-856; p) Y. Yang, L. Zhao, B. Xu, L. Yang, J. Zhang, H. Zhang, J. Zhou, *Bioorg. Chem*. **2016**, *68*, 236-244; q) J. Hu, Y. Wang, Y. Li, L. Xu, D. Cao, S. Song, M. S. Damaneh, X. Wang, T. Meng, Y.-L. Chen, J. Shen, Z. Miao, B. Xiong, *Eur. J. Med. Chem*. **2017**, *137*, 176-195; r) C.-L. Tung, C.-M. Sun, *Tetrahedron Lett*. **2004**, *45*, 1159-1162; s) K. Chanda, J. Kuo, C.-H. Chen, C.-M. Sun, *J. Comb. Chem*. **2009**, *11*, 252-260; t) S. L. Mangold, L. R. Prost, L. L. Kiessling, *Chem. Sci*. **2012**, *3*, 772-777; u) X. Li, D. Wang, J. Wu, W. Xu, *Synth. Commun*. **2005**, *35*, 2553-2560; v) K. Kudo, T. Honda, N. Yamamoto, *Heterocycles* **2015**, *91*, 1591-1602; w) X. Li, D. Wang, J. Wu, W. Xu, *Heterocycles* **2005**, *65*, 2741-2751; x) M. Jørgensen, L. K. Rasmussen, *Int. Patent* 2014139983, **2014**; y) M. Rueping, F. Tato, F. R. Schoepke, *Chem. – Eur. J.* **2010**, *16*, 2688-2691; z) X. Zhang, B. Xu, M.-H. Xu, *Org. Chem. Front.* **2016**, *3*, 944-948; aa) Z.-Y. Xue, Y. Jiang, X.-Z. Peng, W.-C. Yuan, X.-M. Zhang, *Adv. Synth. Catal.* **2010**, *352*, 2132-2136; ab) M. Imanishi, M. Sonoda, H. Miyazato, K. Sugimoto, M. Akagawa, S. Tanimori, *ACS Omega* **2017**, *2*, 1875-1885; ac) S. Tanimori, T. Nishimura, M. Kirihata, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 4119-4121.

[9] K. S. Kanyiva, M. Horiuchi, T. Shibata, *Eur. J. Org. Chem*. **2018**, 1067-1070.

[10] In addition to all those methods, other methods are also available to obtain racemic dihydroquinoxalinones, such as Grignard reactions between quinoxalinones and alkylmagnesium halide and reductive ring-opening of 2-phenyl-*1'H,5H*-spiro[oxazole-4,2'-quinoxalin]-3'(4'*H*)-ones. See: a) A. Marxer, U. Salzmann and F. Hofer, *Helv. Chim. Acta* **1971**, *54*, 2507-2516; b) I. Mušič and B. Verček, *Heterocycles* **2012**, *86*, 719-725.

[11] S. Enthaler, in *Comprehensive Inorganic Chemistry II* (Second Edition) (Ed.: K. Poeppelmeier), Elsevier, Amsterdam, **2013**, pp. 549-562.

[12] a) T. Ollevier, *Catal. Sci. Technol*. **2016**, *6*, 41-48; b) H. Xu, L. Li, C. Lin, W. Kou, Z. Ling, Z. Xu, L. Rong, *Synthesis* **2018**, *50*, 583-592; c) K. S. Egorova, V. P. Ananikov, *Organometallics* **2017**, *36*, 4071-4090; d) M. Li, V. Carreras, A. Jalba, T. Ollevier, *Org. Lett.* **2018**, *20*, 995-998; e) J. Kraïem, T. Ollevier, *Green Chem*. **2017**, *19*, 1263-1267; f) W. Xu, T. Ollevier, F. Kleitz, *ACS Catal*. **2018**, *8*, 1932-1944.

[13] Y.-J. Cherng, *Tetrahedron* **2000**, 56, 8287-8289.

[14] For (*o*-nitrophenyl)-*L*-asparagine (62%), the product was more difficult to extract. For the synthesis of (*o*-nitrophenyl)-*L*-glutamine (40%), the amide group hydrolyzed and the reaction mixture was difficult to purify. For *N*-(o-nitrophenyl)-3,4-dihydroxy-*L*-phenylalanine (28%), the phenol groups competed with the amino group to do the S_NAr towards *o*-nitro-fluorobenzene, resulting in mono- and disubstituted by-products on the phenol ring.

[15] a) O.-J. Park, S.-H. Lee, T.-Y. Park, S.-W. Lee, K.-H. Cho, *Tetrahedron: Asymmetry* **2005**, *16*, 1221-1225; b) C. C. Musonda, V. Yardley, R. C. Carvalho de Souza, K. Ncokazi, T. J. Egan, K. Chibale*, Org. Biomol. Chem*. **2008**, *6*, 4446-4451.

[16] P. J. Dunn, S. Galvin, K. Hettenbach, *Green Chem*. **2004**, 6, 43-48.

[17] P.-D. Ren, S.-F. Pan, T.-W. Dong, S.-H. Wu, *Synth. Commun*. **1995**, *25*, 3799-3803.

[18] S. Chandrappa, K. Vinaya, T. Ramakrishnappa, K. S. Rangappa, *Synlett* **2010**, 3019-3022.

[19] M. Shevlin, X. Guan, T. G. Driver, *ACS Catal*. **2017**, *7*, 5518-5522.

[20] D. Prajapati, H. N. Borah, J. S. Sandhu, A. C. Ghosh, *Synth. Commun*. **1995**, *25*, 4025-4028.

[21] H. N. Borah, D. Prajapati, J. S. Sandhu, A. C. Ghosh, *Tetrahedron Lett*. **1994**, *35*, 3167-3170.

[22] a) S. Gowda, D. C. Gowda, *Indian J. Chem*. **2003**, *42B*, 180-183; b) G. R. Srinivasa, K. Abiraj, D. C. Gowda, *Indian J. Chem*. **2003**, *42B*, 2885-2887.

[23] The reaction time of the first step (S_NAr) was extended from 16 h to 72 h; the reaction time of the second step (synthesis of amino acid ester) was extended from 8 h to 24 h; the reaction time of the third step (reductive cyclization) was extended from 16 h to 40 h.

[24] S. Tanimori, M. Kirihata, *Jpn. Kokai Tokkyo Koho* 2011020992, **2011**.

[25] A. Noriyoshi, S. Yu, I. Kotaro, O. Takeshi, *Adv. Synth. Catal.* **2013**, *355*, 2769-2774.

[26] A. E. Adegoke, B. I. Alo, F. O. Ogunsulire, *J. Heterocycl. Chem*. **1983**, *20*, 1509-1512.

[27] A. Patel, H. J. Smith, R. D. E. Sewell, M. Ahmadi, *Chem. Ind. (London)* **1991**, 630-631.

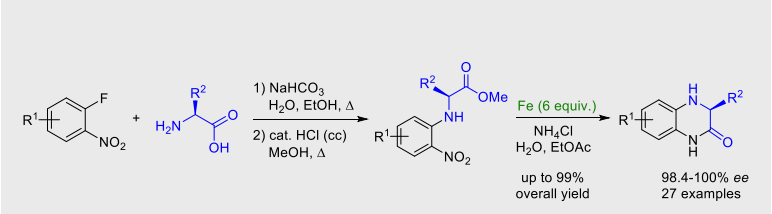
[28] K. Azuma, S. Suzuki, S. Uchiyama, T. Kajiro, T. Santa, K. Imai, *Photochem. Photobiol. Sci*. **2003**, *2*, 443-449.

10.1002/ejoc.201801639

WILEY-VCH

Entry for the Table of Contents

FULL PAPER



A general and efficient synthesis of dihydroquinoxalinones has been developed. The reductive cyclization of *N*-(*o*-nitroaryl)amino esters was performed by using iron and zinc metal under mild conditions in a water/ethyl acetate mixture. The final products were obtained in moderate to high yields and high enantiomeric purity.

Enantiopure Dihydroquinoxalinones*

*Dazhi Li, Thierry Ollevier**

Page No. – Page No.

Iron- and Zinc-mediated Synthetic Approach to Enantiopure Dihydroquinoxalinones