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pH-Regulated transfer hydrogenation of quinoxalines with a Cp*Ir–diamine catalyst in aqueous media

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ABSTRACT

The combination of $[Cp^*IrCl_2]_2$ with *N*-(2-aminoethyl)-4-(trifluoromethyl)benzenesulfonamide constitutes an efficient catalyst for selective transfer hydrogenation of a variety of quinoxalines in water with HCOONa as the hydrogen source, affording the corresponding tetrahydroquinoxalines in good to excellent yields. The catalyst is air-stable, and the reduction could be performed without nitrogen protection. The aqueous phase reduction is shown to be highly pH-dependent, with acidic pH leading to better results. There exits a pH window for optimum rate, and the use of HOAc/NaOAc buffer solution is essential for maintaining a stable pH during the reaction.

1. Introduction

1,2,3,4-Tetrahydroquinoxaline derivatives are a class of useful organic compounds with a wide range of important biological properties, and recent studies have disclosed that compounds containing this heterocyclic unit display great potential for pharmaceutical applications.[1,2] For example, it has been reported that 1,2,3,4-tetrahydroquinoxalines could serve as models for tetrahydrofolic acid,[1a,b] potent vasopressin V2 receptor antagonists,[1f] promising cholesteryl ester transfer protein inhibitors,[1g] prostaglandin D2 receptor antagonists or therapeutic agents for increasing renal fluid flow.[1h] Furthermore, it is notable that 1,2,3,4-tetrahydroquinoxalines are known as promising dyes and cell adhesion agents.[2] Accordingly, significant efforts have been devoted to the efficient construction of these useful heterocycles, and a variety of synthetic methods have been developed.[3–9] Among them, the selective reduction of the heterocyclic ring in readily accessible quinoxalines appears to be the most convenient. A number of reducing reagents, such as lithium aluminum hydride,[3a] sodium borohydide,[3b] titanium chloride,[3c] indium powder,[3d] and borane[3e] have proved to be effective in reducing quinoxaline derivatives into 1,2,3,4-tetrahydroquinoxalines. Direct catalytic hydrogenation of quinoxalines with molecular hydrogen using heterogeneous metal catalysts has also been well-established.[4] However, homogeneous hydrogenation, especially the asymmetric version, is still the subject of a massive research effort.[5] Alternatively, 1,2,3,4-tetrahydroquinoxalines could be prepared by Pd-catalyzed tandem allylation of *o*-phenylenediamines with 1,4-butene diol or acetates,[6] Lewis-acid promoted addition of allyl stannanes to *o*-quinonediimines,[7] Ir-catalyzed N-heterocyclization of anilino alcohols[8] and some domino processes involving suitably substituted nitroarenes.[9]

Recently transition-metal catalyzed transfer hydrogenation using a hydrogen donor other than molecular hydrogen has received increasing attention, because of its versatility, operational simplicity, and safety.[10] Although the studies are mainly concerned with reduction of ketones and imines, some progress has been made in the transfer reduction of nitrogen-containing heteroaryl compounds, such as quinolines,[11] isoquinolines,[12] pyridines,[11c,e,12a] and pyrazines.[12a] However, transition-metal catalyzed transfer hydrogenation of quinoxaline derivatives has been less explored, with only two examples available in the literature.[11a,h] In 1984, Watanabe et al. found that in the presence of $RuCl_2(PPh_3)_3$, quinoxaline could be regio- and chemo-selectively reduced into

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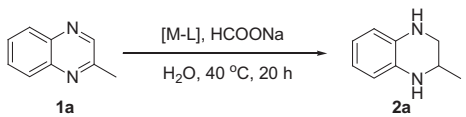
1,2,3,4-tetrahydroquinoxaline by formic acid in benzene; but a high temperature (180 °C) was required to ensure a good conversion.[11a] Very recently, Wills et al. revealed that a Ru–diamine catalyst, while effective for transfer hydrogenation of quinolines, could only give a 17% conversion for the reduction of quinoxaline in the $HCOOH/NEt_3$ azeotrope in 48 h.[11h] In both of these reports, only one quinoxaline substrate was attempted. Given the importance of 1,2,3,4-tetrahydroquinoxalines, it is highly desirable to develop a more efficient and greener method for transfer hydrogenation of quinoxalines. Following our continuing effort for reduction of various heteroaromatic compounds,[11g,13,14] we became interested in exploring the transition-metal catalyzed transfer hydrogenation of quinoxalines. Herein we wish to report that regio- and chemoselective transfer hydrogenation of quinoxaline derivatives can be carried out efficiently in an aqueous HOAc/NaOAc buffer solution in the presence of an Ir–diamine catalyst using HCOONa as the hydrogen donor, and good to excellent yields have been obtained for a number of substrates. It is notable that the reduction could be performed in air without nitrogen protection.

2. Results and discussion

Recent studies have disclosed that the water-insoluble catalysts created from $[(p\text{-cymene})_2RuCl_2]_2$ or $[Cp^*MCl_2]_2$ (M=Ir, Rh) and monotosylated diamine ligands, which were originally designated for organic solvents, could work well to catalyze the transfer reduction of ketones, aldehdyes, and nitroalkenes by HCOONa in neat water, with no modification of ligands required.[14,15] Of particular note is that Rh-catalyzed asymmetric transfer hydrogenation of quinolines could proceed smoothly in a HOAc/NaOAc buffer solution employing HCOONa as the hydrogen donor without organic solvent, providing excellent yields and enantioselectivities for a wide range of substrates.[11g] The reaction is pH dependent, however, and the use of the HOAc/NaOAc buffer solution is very important due to its strong ability to suppress the pH fluctuation. It is believed that the quinolines are reduced by a Rh–H hydride through an ionic mechanism, in which the quinolines are preactivated by protonation under the acidic condition.

Inspired by these successful reports, we decided to first evaluate the transfer reduction of 2-methylquinoxaline **1a** with water as the reaction medium and HCOONa as the hydrogen source. Three metal complexes, $[Cp^*IrCl_2]_2$, $[Cp^*RhCl_2]_2$, and $[(p\text{-cymene})_2RuCl_2]_2$, were initially chosen as the catalysts with no additional ligands, and the reaction was carried out under a nitrogen atmosphere at 40 °C. As shown in Table 1, no reaction was observed after 20 h in the presence of the metal catalyst (Table 1, entries 1–3). In the hope to observe catalytic activity, a ligand was then used. However, there was still no conversion with the addition of the readily available ethylenediamine (en) (Table 1, entries 4–6). Considering the remarkable performance of monosulfonylated diamine ligands in transfer hydrogenations,[10] we then investigated the catalytic effect of monotosylated ethylenediamine (**3a**). Whilst the combination of $[(p\text{-cymene})_2RuCl_2]_2$ with ligand **3a** led to no reaction (entry 8), and only traces of product was found in the case of catalyst Rh-**3a** (entry 7), the catalyst Ir-**3a** provided a conversion of 17% (entry 9). It was noted that the reaction was highly regioselective to transform **1a** into the desired 2-methyl tetrahydroquinoxaline; side products were not observed.

Table 1
Optimization of the reaction conditions for transfer hydrogenation of 2-methylquinoxaline **1a**[a]



Entry	Metal precursors	Ligand	Convn. (%)[b]
1	$[Cp^*RhCl_2]_2$	None	0
2	$[(p\text{-Cymene})_2RuCl_2]_2$	None	0
3	$[Cp^*IrCl_2]_2$	None	0
4	$[Cp^*RhCl_2]_2$	en	0
5	$[(p\text{-Cymene})_2RuCl_2]_2$	en	0
6	$[Cp^*IrCl_2]_2$	en	0
7	$[Cp^*RhCl_2]_2$	**3a**	2
8	$[(p\text{-Cymene})_2RuCl_2]_2$	**3a**	0
9	$[Cp^*IrCl_2]_2$	**3a**	17

[a] All reactions were performed with **1a** (0.5 mmol), metal precursor (2.5 μmol), ligand (6 μmol), HCOONa (5 mmol), and water (5 mL) at 40 °C in 20 h.
[b] The conversions were determined by ^1H NMR.

Under present conditions, the initial pH value of the reaction mixture was about 8. In our previous study, the transfer hydrogenation of quinolines using the Rh–diamine complex as catalyst was also sluggish under the similar basic conditions; however, switching the reaction medium from neat water to a solution buffered at pH 5 could greatly enhance the reactivity of quinolines.[11g] We thus reasoned that the pH value of the reaction medium might also have a critical effect on the reaction rate in the closely related transfer reduction of quinoxlines, and the HOAc/NaOAc solution might act as an effective reaction medium due to its buffering capability. We therefore examined the effect of the pH value of the solution on the reduction of **1a** in a 2 M HOAc/NaOAc buffer solution with the catalyst generated in situ from **3a** and $[Cp^*IrCl_2]_2$, and the pH value was adjusted by changing the ratio of HOAc and NaOAc while keeping the concentration of $[AcO^-]$ constant. As shown in Fig. 1, the reduction of **1a** with Ir-**3a** was indeed strongly pH-dependent. The reaction rate versus pH showed a volcano curve, reaching its maximum at pH 5.5. The pH window for optimum rates is narrow, and deviating from pH 5.5 led to a rapid decrease in the reduction rate. This is reminiscent of the observations made in the Rh-catalyzed aqueous transfer hydrogenation of quinolines and ketones,[11g,14] indicating that acidic activation of **1a** is required. It is speculated that the reduction of **1a** probably proceeds via an ionic pathway, where an Ir–H is transferred to the protonated instead of neutral quinoxaline. The ionic mechanism has been suggested by several groups in the transition-metal catalyzed hydrogenation or transfer hydrogenation of imines and quinolines.[5i,11g,13f,16]

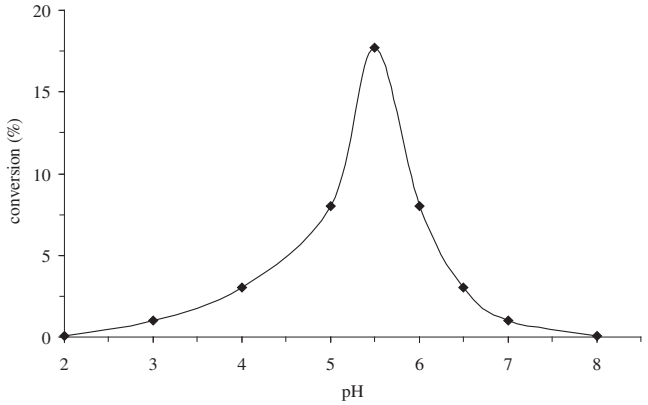


Fig. 1. Effect of the initial pH value of the buffer solution on the transfer hydrogenation of **1a** catalyzed by Ir-**3a**. Reactions were conducted on a 0.5 mmol scale in a 2 M HOAc/NaOAc buffer solution for 10 min at 40 °C.

Under the optimized pH value, however, the reduction of **1a** failed to reach completion even after prolonging the reaction time to 20 h. This raised the question of whether the pH value of the HOAc/NaOAc buffer varied significantly during the reaction. Monitoring the reaction progress was then carried out. As shown in Fig. 2, the initial reduction proceeded smoothly when the reaction

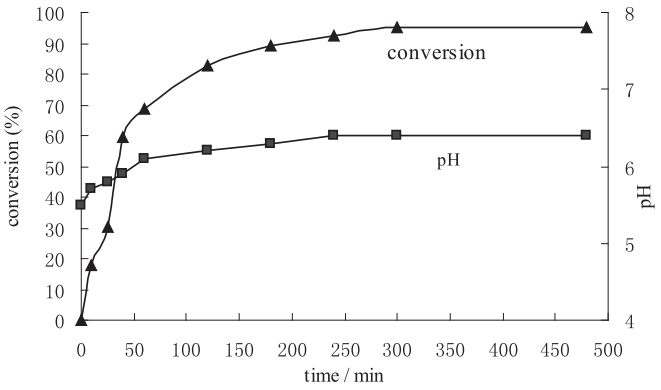


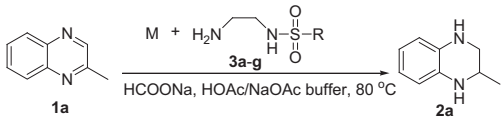
Fig. 2. Conversion (▲) and pH value (■) with respect to time in the transfer hydrogenation of **1a** catalyzed by Ir-**3a**. Reactions were conducted on a 0.5 mmol scale in a 2 M HOAc/NaOAc buffer solution at 40 °C.

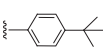
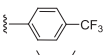
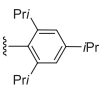
started at pH 5.5, but the pH value gradually increased. After about 2 h, the reaction became sluggish. The reaction stopped completely in 5 h with a 95% conversion, and the pH value of the reaction medium changed from 5.5 to 6.4. Given the sensitivity of the reaction rate pH (Fig. 1), this pH rise is quite likely to be responsible to the decrease in reactivity, and it appears that the buffer capacity of 2 M HOAc/NaOAc is insufficient. Expectedly, when we increased the concentration of HOAc/NaOAc buffer from 2 M to 5 M, the reaction went to completion in 2 h. This enhanced reactivity may be attributed to the increasing buffer capacity of the HOAc/NaOAc solution, which reduced the pH fluctuation during the reaction. Gratifyingly, when increasing the reaction temperature to 80 °C, the reaction could give rise to a 61% conversion only in 0.25 h (Table 2, entry 1). For comparison, the performance of Rh-**3a** and Ru-**3a** was also tested; but only lower conversions were obtained under otherwise identical conditions (Table 2, entries 2 and 3).

In order to further improve the reduction efficiency, we then examined the performance of different RSO_2—en ligands. As shown in Table 2, the R group of the sulphonamide is essential for the activity of the catalyst. When R was a phenyl group, only 27% conversion was observed, but the 4-*tert*-butylphenyl-substituted ligand **3c** produced a good result (Table 2, entries 4 and 5). The use of sterically demanding ligands resulted in poor results (Table 2, entries 7 and 8), and employing the simple ligand CH_3SO_2—en led to no enhancement in reactivity (Table 2, entry 9). Among the ligands examined, the electron-deficient **3d** having a 4-trifluoromethylphenyl substituent proved to be the best choice, providing a full conversion in 0.25 h (Table 2, entry 6). It is notable that the catalyst maintained the same activity when performing the reduction in air without degassing, circumventing the need for nitrogen protection or degassed solvent.

With these encouraging results in hand, we then turned to explore the scope of this chemistry using a series of quinoxaline derivatives as substrates under the reaction conditions optimized above. The 2-alkylated substrates were readily synthesized by Fe-catalyzed coupling reaction of 2-chloroquinoxaline with Grignard reagents.[5h] The cyclization—oxidation of benzene-1,2-diamine with α-bromoketones led to 2-arylated quinoxalines.[17a] The 2-styryl-substituted quinoxalines were prepared via the condensation reaction of 2-methylquinoxaline and corresponding aromatic aldehydes.[17b] As shown in Table 3, all 2-alkylated quinoxalines reacted well to provide the desired products in excellent yields; but the reaction time varied with the length of the side chain (Table 3, entries 1–8, 10). It was found that longer reaction time was needed for the substrate bearing a sterically demanding alkyl group at the 2-position (Table 3, entry 6). The presence of substituents at the 6- and 7-positions of the quinoxaline framework had no obvious

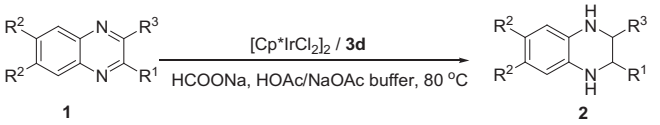
Table 2
Transfer hydrogenation of 2-methylquinoxaline **1a**[a]



Entry	Metal precursors	3	R	Convn. (%)[b]
1	$[Cp^*IrCl_2]_2$	**3a**		61
2	$[Cp^*RhCl_2]_2$	**3a**		44
3	$[(p\text{-Cymene})_2RuCl_2]_2$	**3a**		34
4	$[Cp^*IrCl_2]_2$	**3b**		27
5	$[Cp^*IrCl_2]_2$	**3c**		91
6	$[Cp^*IrCl_2]_2$	**3d**		>99
7	$[Cp^*IrCl_2]_2$	**3e**		66
8	$[Cp^*IrCl_2]_2$	**3f**		63
9	$[Cp^*IrCl_2]_2$	**3g**	CH_3	22

[a] All reactions were performed with **1a** (0.5 mmol), metal precursor (2.5 μmol), ligand (6 μmol), HCOONa (5 mmol), and 5 M buffer (5 mL) at 80 °C in 0.25 h.
[b] The conversions were determined by ^1H NMR.

Table 3
Transfer hydrogenation of substituted quinoxalines **1** catalyzed by Ir-**3d**[a]



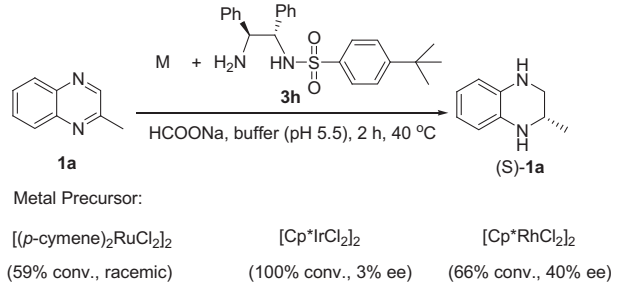
Entry	$R^1/R^2/R^3$	Time (h)	Yield (%)[b]
1	Methyl/H/H (**1a**)	0.25	96
2	Ethyl/H/H (**1b**)	1	97
3	*n*-Butyl/H/H (**1c**)	1	93
4	Isobutyl/H/H (**1d**)	2	96
5	Hexyl/H/H (**1e**)	2	97
6	Cyclohexyl/H/H (**1f**)	6	92
7	Methyl/methyl/H (**1g**)	1	97
8	Ethyl/methyl/H (**1h**)	1	96
9	H/H/H (**1i**)	0.25	97
10	Methyl/H/methyl (**1j**)	4	94
11[c]	Phenyl/H/H (**1k**)	10	97
12[c]	4-Fluoro-phenyl/H/H (**1l**)	10	97
13[c]	4-Chloro-phenyl/H/H (**1m**)	10	95
14[c]	4-Bromo-phenyl/H/H (**1n**)	10	95
15[c]	4-MeO-phenyl/H/H (**1o**)	10	97
16[c]	2-MeO-phenyl/H/H (**1p**)	10	94
17[c]	*p*-Tolyl/H/H (**1q**)	10	93
18[c]	4-Biphenyl/H/H (**1r**)	10	91
19[d]	Styryl/H/H (**1s**)	12	95
20[d]	2-Cl-styryl/H/H (**1t**)	12	96
21[d]	3-NO_2-styryl/H/H (**1u**)	12	95

[a] All reactions were performed with quinoxaline **1** (0.5 mmol), $[Cp^*IrCl_2]_2$ (2.5 μmol), **3d** (6 μmol), HCOONa (5 mmol), and 5 M HOAc/NaOAc buffer (5 mL, pH=5.5) at 80 °C.
[b] Isolated yield after column chromatography.
[c] The reaction was carried out at pH 4.3 in 5 M HOAc/NaOAc (5 mL) buffer with EtOAc (0.3 mL).
[d] The reaction was carried out at pH 4.5 in 5 M HOAc/NaOAc buffer.

effect on the catalytic reactivity (Table 3, entries 7 and 8). The simple quinoxaline was also proved to be a viable substrate, giving rise to the product in 97% yield (Table 3, entry 9). Interestingly, 2,3-disubstituted substrate could be stereoselectively reduced into tetrahydroquinoxaline in high yield, and only the cis-isomer was observed (Table 3, entry 10).

However, under the conditions described above the reduction of 2-aryl substituted quinoxalines proved to be problematic. For example, when the substrate **1k** was subjected to transfer reduction, only 20% conversion was attained in 24 h. Delightfully, when lowering the pH value of the buffer from 5.5 to 4.3 and adding EtOAc as the co-solvent, the reduction of **1k** could finish in 10 h with a nearly quantitative yield (Table 3, entry 11). The addition of co-solvent is probably due to the relatively poor aqueous solubility of **1k**. Similarly, high yields were observed in the reduction of other 2-aryl substituted substrates regardless of the nature of the substituents in the benzene ring (Table 3, entries 12–18). This resembles the observation made in the transfer hydrogenation of 2-aryl substituted quinolines in HOAc/NaOAc solution.[11g] It is noticed that, when adjusting the pH of HOAc/NaOAc buffer to 4.5, 2-styryl-substituted quinoxalines could also undergo selective reduction with retention of the carbon–carbon double bond, and the substituent on the styryl ring showed no significant influence on the catalytic reactivity (Table 3, entries 19–21). This is synthetically useful, since the tolerated double bond can be used for further functionalization. Similar observations have been found in Ir-catalyzed hydrogenation of 2-styryl-substituted quinoxalines.[5g]

We next investigated the asymmetric transfer hydrogenation of quinoxalines in the presence of a chiral ligand **3h** (*N*-((1*S*,2*S*)-2-amino-1,2-diphenylethyl)-4-*tert*-butylbenzenesulfonamide) in the 5 M HOAc/NaOAc buffer at 40 °C. The results were disappointing. With **1a** as the model substrate, $[(p\text{-cymene})_2RuCl_2]_2$ gave a racemic product, and only 3% ee was observed when using Ir-**3h** as the catalyst. The best enantioselectivity was achieved in the case of $[Cp^*RhCl_2]_2$, the ee being 40% (Scheme 1). With Rh-**3h** as the catalyst, both **1e** and **1k** could be completely reduced in 24 h in the HOAc/NaOAc buffer (pH 5.5 for **1e** and pH 4.3 with EtOAc as the co-solvent for **1k**); the enantioselectivity was again low, however, at 20% and 5% ee, respectively.



Scheme 1. Asymmetric transfer hydrogenation of **1a**.

3. Conclusions

In conclusion, we have developed a highly efficient, Ir-catalyzed transfer hydrogenation protocol for the reduction of quinoxalines with HCOONa as the hydrogen source in aqueous media. The reduction is pH dependent, showing a narrow pH window for optimum rate, and the use of a HOAc/NaOAc buffered solution is important to suppress pH fluctuation during the reaction. The catalyst is generated in situ, and is stable to air. A number of quinoxaline derivatives could be smoothly reduced under the buffered conditions, affording good to excellent yields with good functional tolerance. This mild and operationally simple method offers a useful route to tetrahydroquinoxalines, and the development of more efficient chiral catalyst systems is ongoing in our laboratory.

4. Experimental section

4.1. General

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Model Avance DMX 400 Spectrometer (^1H 400 MHz and ^{13}C 106 MHz, respectively). Chemical shifts (δ) are given in ppm and are referenced to residual solvent peaks. Water was distilled prior to use. THF was dried over sodium and distilled prior to use. CH_3CN was dried over P_2O_5 and distilled prior to use. Quinoxaline (**1i**), 2-methylquinoxaline (**1a**), and 2,3-dimethylquinoxaline (**1j**) were purchased from Aldrich, and used as received. Other 2-alkyalted quinoxalines, 2-arylated quinoxalines, and 2-styryl substituted quinoxalines were prepared according to the literature procedures.[5h,17,18] All other chemicals were used as received from Aldrich or Acros without further purification.

4.2. General procedure for synthesis of mono-*N*-sulfonated ethylenediamines

A solution of sulfonyl chloride (10 mmol) in CH_2Cl_2 (25 mL) was slowly added to a stirred solution of ethylenediamine (6.0 g, 100 mmol) in dry CH_2Cl_2 (25 mL). The resulting mixture was stirred for 15 min, washed twice with water (25 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the monosulfonylated ethylenediamine was obtained after flash chromatography (CH_2Cl_2/methanol).

*4.2.1. N-(2-Aminoethyl)-4-methylbenzenesulfonamide(**3a**)*[15d]. White solid, mp 106–107 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J=8.3 Hz, 2H), 7.31 (d, J=8.3 Hz, 2H), 2.96 (q, J=5.4 Hz, 2H), 2.78 (q, J=5.9 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 144.3, 137.9, 130.7, 128.0, 46.3, 41.8, 22.5; HRMS (ESI) calcd for $C_9H_{15}N_2O_2S$ $[M+H]^+$ 215.0849, found 215.0851.

*4.2.2. N-(2-Aminoethyl)benzenesulfonamide(**3b**).* White solid, mp 67–69 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.48–7.50 (m, 1H), 7.42–7.46 (m, 2H), 2.90–2.92 (q, J=5.9 Hz, 2H), 2.72–2.75 (q, J=5.9 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 140.7, 133.4, 129.9, 127.7, 46.0, 41.8; HRMS (ESI) calcd for $C_8H_{13}N_2O_2S$ $[M+H]^+$ 201.0692, found 201.0699.

*4.2.3. N-(2-Aminoethyl)-4-tert-butylbenzenesulfonamide(**3c**).* White solid, mp 79–81 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J=8.7 Hz, 2H), 7.49 (d, J=8.7 Hz, 2H), 3.02 (q, J=5.1 Hz, 2H), 2.89 (q, J=6.2 Hz, 2H), 1.32 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.3, 137.6, 127.9, 127.1, 45.5, 41.7, 36.1, 32.0; HRMS (ESI) calcd for $C_{12}H_{21}N_2O_2S$ $[M+H]^+$ 257.1318, found 257.1323.

*4.2.4. N-(2-Aminoethyl)-4-(trifluoromethyl)benzenesulfonamide(**3d**).* White solid, mp 103–105 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J=8.2 Hz, 2H), 7.78 (d, J=8.2 Hz, 2H), 2.99–3.01 (m, 2H), 2.82–2.85 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 144.6, 135.4, 128.5, 127.3, 127.2, 46.1, 41.7; HRMS (ESI) calcd for $C_9H_{12}F_3N_2O_2S$ $[M+H]^+$ 269.0566, found 269.0573.

*4.2.5. N-(2-Aminoethyl)-2,4,6-triisopropylbenzenesulfonamide (**3e**).* White solid, mp 120–122 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (s, 2H), 4.10–4.20 (m, 2H), 3.00–3.02 (m, 2H), 2.83–2.90 (m, 3H), 1.23–1.26 (m, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.5, 151.2, 133.1, 124.7, 45.4, 41.7, 35.1, 30.5, 25.9, 24.5; HRMS (ESI) calcd for $C_{17}H_{31}N_2O_2S$ $[M+H]^+$ 327.2101, found 327.2105.

*4.2.6. N-(2-Aminoethyl)-2,3,4,5,6-pentamethylbenzenesulfonamide(**3f**).* White solid, mp 129–132 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.87–2.90 (m, 2H), 2.78–2.81 (m, 2H), 2.60 (s, 6H), 2.27 (s, 3H), 2.23 (s, 6H)

ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 140.3, 136.7, 135.7, 135.1, 45.9, 41.7, 19.9, 18.7, 18.1; HRMS (ESI) calcd for $C_{13}H_{23}N_2O_2S$ $[M+H]^+$ 271.1475, found 271.1478.

*4.2.7. N-(2-Aminoethyl)methanesulfonamide(**3g**)*[15d]. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.16 (q, J=5.6 Hz, 2H), 2.97 (s, 3H), 2.90 (q, J=5.6 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 45.5, 41.4, 40.2; HRMS (ESI) calcd for $C_3H_{11}N_2O_2S$ $[M+H]^+$ 139.0536, found 139.0541.

4.3. Analysis of the substituted quinoxaline substrates

*4.3.1. 2-Ethylquinoxaline (**1b**)*[5g,h,18a]. Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.03–8.08 (m, 2H), 7.70–7.74 (m, 2H), 3.06 (q, J=7.6 Hz, 2H), 1.44 (q, J=7.6 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 159.3, 146.4, 142.9, 142.0, 130.7, 129.9, 129.7, 129.6, 30.4, 14.2; HRMS (ESI) calcd for $C_{10}H_{11}N_2$ $[M+H]^+$: 159.0917, found: 159.0921.

*4.3.2. 2-Butylquinoxaline (**1c**)*[5g,h,18b]. Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.02–8.08 (m, 2H), 7.69–7.74 (m, 2H), 3.00–3.03 (m, 2H), 1.80–1.85 (m, 2H), 1.43–1.49 (m, 2H), 0.95–0.99 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.3, 146.5, 142.9, 141.9, 130.6, 129.9, 129.6, 129.5, 36.9, 32.3, 23.3, 14.6; HRMS (ESI) calcd for $C_{12}H_{15}N_2$ $[M+H]^+$: 187.1230, found: 187.1236.

*4.3.3. 2-Isobutylquinoxaline (**1d**)*[5g,h]. Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.04–8.08 (m, 2H), 7.69–7.74 (m, 2H), 2.88–2.90 (d, J=7.3 Hz, 2H), 2.22–2.28 (m, 1H), 1.01 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.6, 146.9, 142.9, 141.9, 130.6, 129.9, 129.7, 129.6, 46.1, 30.0, 23.2; HRMS (ESI) calcd for $C_{12}H_{15}N_2$ $[M+H]^+$: 187.1230, found: 187.1234.

*4.3.4. 2-Hexylquinoxaline (**1e**).* Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.97–8.02 (m, 2H), 7.60–7.68 (m, 2H), 2.92–2.96 (m, 2H), 1.74–1.82 (m, 2H), 1.33–1.40 (m, 2H), 1.22–1.31 (m, 4H), 0.80–0.84 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.5, 146.7, 143.0, 142.0, 130.7, 130.0, 129.7, 129.4, 37.4, 32.5, 30.4, 29.9, 23.4, 14.9; HRMS (ESI) calcd for $C_{14}H_{19}N_2$ $[M+H]^+$: 215.1543, found: 215.1549.

*4.3.5. 2-Cyclohexylquinoxaline (**1f**).* Brown solid, mp 49–51 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.01–8.06 (m, 2H), 7.65–7.73 (m, 2H), 2.91–2.98 (m, 1H), 2.00–2.04 (m, 2H), 1.88–1.93 (m, 2H), 1.64–1.74 (m, 2H), 1.31–1.51 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 162.1, 146.0, 143.1, 142.3, 130.7, 130.0, 129.9, 129.8, 45.9, 33.2, 27.3, 26.8. HRMS (ESI) calcd for $C_{14}H_{17}N_2$ $[M+H]^+$: 213.1386, found: 213.1401.

*4.3.6. 2,6,7-Trimethylquinoxaline (**1g**)*[5g]. White solid, mp 112–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.77 (s, 1H), 7.72 (s, 1H), 2.71 (s, 3H), 2.45 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.5, 145.8, 141.8, 141.2, 140.7, 140.0, 129.0, 128.5, 23.2, 21. 1, 20.9; HRMS (ESI) calcd for $C_{11}H_{13}N_2$ $[M+H]^+$: 173.1073, found: 173.1079.

*4.3.7. 2-Ethyl-6,7-dimethylquinoxaline (**1h**)*[5g]. White solid, mp 115–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.78 (s, 2H), 2.96–3.02 (m, 2H), 2.46 (s, 6H), 1.38–1.42 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.2, 145.3, 141.8, 141.1, 140.9, 139.9, 128.9, 128.7, 30.3, 21.1, 20.9, 14.3; HRMS (ESI) calcd for $C_{12}H_{15}N_2$ $[M+H]^+$: 187.1230, found: 187.1237.

*4.3.8. 2-Phenylquinoxaline (**1k**)*[5g,h,18b]. Red solid, mp 78–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.11–8.21 (m, 4H), 7.72–7.81 (m, 2H), 7.51–7.60 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.6, 144.1, 143.1, 142.4, 137.6, 131.1, 130.9, 130.4, 130.3, 130.0, 129.9, 128.3; HRMS (ESI) calcd for $C_{14}H_{11}N_2$ $[M+H]^+$: 207.0917, found: 207.0920.

*4.3.9. 2-(4-Fluorophenyl)quinoxaline (**1l**)*[18b]. White solid, mp 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.19–8.23 (m, 2H), 8.11–8.15 (m, 2H), 7.73–7.82 (m, 2H), 7.24–7.28 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 151.7, 143.9, 143.2, 142.5, 133.9, 131.4, 130.6, 130.5, 130.4, 130.1, 117.3, 117.1; HRMS (ESI) calcd for $C_{14}H_{10}FN_2$ $[M+H]^+$: 225.0823, found: 225.0829.

*4.3.10. 2-(4-Chlorophenyl)quinoxaline (**1m**).* White solid, mp 133–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (s, 1H), 8.09–8.14 (m, 4H), 7.72–7.78 (m, 2H), 7.50–7.52 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 151.5, 143.89, 143.1, 142.6, 137.5, 136.1, 131.4, 130.7, 130.5, 130.3, 130.1, 128.7; HRMS (ESI) calcd for $C_{14}H_{10}ClN_2$ $[M+H]^+$: 241.0527, found: 241.0533.

*4.3.11. 2-(4-Bromophenyl)quinoxaline (**1n**)*[19]. White solid, mp 119–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.10–8.14 (m, 2H), 8.06–8.08 (m, 2H), 7.73–7.80 (m, 2H), 7.67–7.69 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 151.5, 143.7, 143.1, 143.6, 136.5, 133.3, 131.4, 130.8, 130.5, 130.1, 129.9, 125.9; HRMS (ESI) calcd for $C_{14}H_{10}BrN_2$ $[M+H]^+$: 285.0022, found: 285.0029.

*4.3.12. 2-(4-Methoxyphenyl)quinoxaline (**1o**)*[18b]. White solid, mp 100–101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.15–8.17 (m, 2H), 8.07–8.11 (m, 2H), 7.67–7.76 (m, 2H), 7.05–7.07 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 162.4, 152.34, 148.7, 144.0, 143.2, 142.1, 131.1, 130.3, 130.1, 130.0, 129.9, 115.5, 55.4; HRMS (ESI) calcd for $C_{15}H_{13}N_2O$ $[M+H]^+$: 237.1022, found: 237.1027.

*4.3.13. 2-(2′-Methoxyphenyl)quinoxaline (**1p**)*[5g,18b]. White solid, mp 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H), 8.11–8.14 (m, 2H), 7.89–7.91 (m, 1H), 7.74–7.77 (m, 2H), 7.46–7.50 (m, 1H), 7.14–7.18 (m, 1H), 7.06–7.08 (m, 1H), 3.91 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.2, 152.9, 148.1, 143.5, 141.8, 132.4, 132.2, 130.5, 130.3, 130.1, 129.9, 127.3, 122.3, 112.2, 56.4; HRMS (ESI) calcd for $C_{15}H_{13}N_2O$ $[M+H]^+$: 237.1022, found: 237.1025.

*4.3.14. 2-p-Tolylquinoxaline (**1q**)*[18b]. White solid, mp 89–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.09–8.15 (m, 4H), 7.70–7.79 (m, 2H), 7.35–7.27 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.8, 144.3, 143.3, 142.4, 141.4, 134.9, 131.1, 130.9, 130.5, 130.2, 130.0, 128.4, 22.4; HRMS (ESI) calcd for $C_{15}H_{13}N_2$ $[M+H]^+$: 221.1073, found: 221.1078.

*4.3.15. 2-(Biphenyl-4-yl)quinoxaline (**1r**).* White solid, mp 118–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (s, 1H), 8.29–8.31 (m, 2H), 8.12–8.19 (m, 2H), 7.74–7.82 (m, 4H), 7.68–7.70 (m, 2H), 7.48–7.52 (m, 2H), 7.39–7.42 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.4, 144.3, 144.0, 143.4, 142.6, 141.2, 136.6, 131.3, 130.6, 130.5, 130.1, 129.9, 128.9, 128.8, 128.2, 128.1; HRMS (ESI) calcd for $C_{20}H_{15}N_2$ $[M+H]^+$: 283.1230, found: 283.1235.

*4.3.16. 2-Styrenylquinoxaline (**1s**)*[5g]. Red solid, mp 104–105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.07 (d, J=6.0 Hz, 2H), 7.88 (d, J=16.3 Hz, 1H), 7.71–7.76 (m, 2H), 7.67 (d, J=7.0 Hz, 2H), 7.36–7.45 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 151.4, 145.2, 143.2, 142.4, 141.6, 137.2, 136.8, 131.2, 131.1, 130.0, 129.9, 129.7, 128.3, 126.1; HRMS (ESI) calcd for $C_{16}H_{13}N_2$ $[M+H]^+$: 233.1073, found: 233.1079.

*4.3.17. 2-(3′-Nitro-styryl)-quinoxaline (**1t**)*[5g]. Brown solid, mp 194–195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.51 (s, 1H), 8.19 (d, J=8.1 Hz, 1H), 8.08 (d, J=7.7 Hz, 2H), 7.91–7.95 (m, 2H), 7.72–7.81 (m, 2H), 7.58–7.62 (m, 1H), 7.49 (d, J=16.2 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 151.4, 143.3, 142.4, 134.3, 132.2, 131.1, 130.3, 130.1, 129.9, 129.5, 128.6, 127.4, 126.9, 126.4, 126.1, 124.4; HRMS (ESI) calcd for $C_{16}H_{12}N_3O_2$ $[M+H]^+$: 278.0924, found: 278.0928.

*4.3.18. 2-(2′-Chloro-styryl)-quinoxaline (**1u**)*[5g]. Red solid, mp 113–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.26 (d,

J=16.4 Hz, 1H), 8.08–8.10 (m, 2H), 7.72–7.83 (m, 3H), 7.29–7.46 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 151.0, 144.9, 142.4, 135.1, 134.9, 132.9, 131.1, 130.9, 130.8, 130.7, 130.2, 130.1, 130.0, 129.9, 128.8, 127.7; HRMS (ESI) calcd for $C_{16}H_{12}ClN_2$ $[M+H]^+$: 267.0684, found: 267.0691.

4.4. General procedure for transfer hydrogenation of quinoxalines

A carousel reaction tube containing a magnetic stirring bar and $[Cp^*IrCl_2]_2$ (2 mg, 2.5 μmol), ligand **3d** (1.6 mg, 6 μmol), quinoxaline substrate (0.5 mmol), and HCOONa (340 mg, 5 mmol) in an aqueous solution of HOAc/NaOAc (5 M, 5 mL, pH=5.5) was sealed without degassing. The reaction mixture was stirred at 80 °C for the time indicated in Table 3, then cooled to room temperature and basified with an aqueous solution of KOH. The resulting mixture was extracted with diethyl ether (3×5 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the product was purified by flash column chromatography.

*4.4.1. 2-Methyltetrahydroquinoxaline(**2a**)*[5g,h,j]. Yellow solid, mp 88–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58–6.60 (m, 2H), 6.49–6.52 (m, 2H), 3.63 (br, 2H), 3.50–3.53 (m, 1H), 3.32 (dd, J=10.6, 7.9 Hz, 1H), 3.05 (dd, J=9.6, 2.7 Hz, 1H), 1.19 (d, J=6.3 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.3, 133.9, 119.5, 119.4, 115.3, 115.2, 49.0, 46.5, 20.7; HRMS (ESI) calcd for $C_9H_{13}N_2$ $[M+H]^+$: 149.1073, found: 149.11077.

*4.4.2. 2-Ethyltetrahydroquinoxaline(**2b**)*[5g,h,j]. Yellow solid, mp 67–69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56–6.60 (m, 2H), 6.50–6.53 (m, 2H), 3.63 (br, 2H), 3.38 (dd, J=7.7, 10.6 Hz, 1H), 3.26–3.32 (m, 1H), 3.08 (dd, J=2.8, 10.6 Hz, 1H), 1.49–1.56 (m, 2H), 0.99–1.03 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.3, 134.1, 119.5, 119.3, 115.2, 115.1, 52.4, 47.0, 27.9, 10.7; HRMS (ESI) calcd for $C_{10}H_{15}N_2$ $[M+H]^+$: 163.1230, found: 163.1239.

*4.4.3. 2-Butyltetrahydroquinoxaline(**2c**)*[5g,h,j]. Brown solid, mp 58–59 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56–6.60 (m, 2H), 6.49–6.51 (m, 2H), 3.64 (br, 2H), 3.35–3.38 (m, 2H), 3.04–3.09 (m, 1H), 1.37–1.59 (m, 6H), 0.92–0.95 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.3, 134.2, 119.5, 119.3, 115.2, 115.1, 51.0, 47.5, 34.8, 28.59, 23.6, 14.8; HRMS (ESI) calcd for $C_{12}H_{19}N_2$ $[M+H]^+$: 191.1543, found: 191.1548.

*4.4.4. 2-iso-Butyltetrahydroquinoxaline(**2d**)*[5g,h,j]. Yellow solid, mp 69–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57–6.60 (m, 2H), 6.49–6.52 (m, 2H), 3.64 (br, 2H), 3.33–3.45 (m, 2H), 3.35 (d, J=10.7 Hz, 1H), 3.05 (dd, J=8.0, 10.6 Hz, 1H), 1.73–1.77 (m, 1H), 1.32–1.39 (m, 1H), 0.95–0.98 (m, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.3, 134.2, 119.5, 119.4, 115.3, 115.2, 48.9, 47.8, 44.1, 25.2, 23.9, 23.3; HRMS (ESI) calcd for $C_{12}H_{19}N_2$ $[M+H]^+$: 191.1543, found: 191.1549.

*4.4.5. 2-Hexyltetrahydroquinoxaline(**2e**).* Yellow solid, mp 74–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57–6.60 (m, 2H), 6.49–6.51 (m, 2H), 3.62 (br, 2H), 3.34–3.38 (m, 2H), 3.06–3.09 (m, 1H), 1.31–1.46 (m, 10H), 0.88–0.90 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.3, 134.2, 119.5, 119.3, 115.2, 115.1, 51.0, 47.5, 35.1, 32.5, 30.1, 26.4, 23.3, 14.8; HRMS (ESI) calcd for $C_{14}H_{23}N_2$ $[M+H]^+$: 219.1856, found: 219.1862.

*4.4.6. 2-Cyclohexyl-1,2,3,4-tetrahydroquinoxaline(**2f**).* Yellow solid, mp 105–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57–6.60 (m, 2H), 6.49–6.52 (m, 2H), 3.63 (br, 2H), 3.36–3.84 (m, 1H), 3.12–3.15 (m, 2H), 1.70–1.80 (m, 5H), 1.39–1.48 (m, 1H), 1.03–1.30 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.6, 134.2, 119.5, 119.1, 115.1, 115.0, 55.9, 44.7, 41.5, 29.9, 29.7, 27.2, 26.9, 26.8; HRMS (ESI) calcd for $C_{14}H_{21}N_2$ $[M+H]^+$: 217.1699, found: 217.1704.

*4.4.7. 2,6,7-Trimethyltetrahydroquinoxaline (**2g**)*[5g,j]. Yellow solid, mp 118–119 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33–6.34 (s, 2H), 3.38–3.49 (m, 3H), 3.27–3.30 (dd, J=8.1, 10.7 Hz, 1H), 2.97–3.02 (dd, J=2.4, 10.7 Hz, 1H), 2.10 (s, 6H), 1.17–1.18 (d, J=6.3 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 132.2, 131.7, 127.3, 127.2, 117.1, 117.0, 49.4, 46.8, 20.6, 19.6; HRMS (ESI) calcd for $C_{11}H_{17}N_2$ $[M+H]^+$: 177.1386, found: 177.1389.

*4.4.8. 2-Ethyl-6,7-dimethyltetrahydroquinoxaline(**2h**)*[5g,j]. Yellow solid, mp 122–123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.34 (s, 2H), 3.48 (br, 2H), 3.34 (dd, J=7.9, 10.6 Hz, 1H), 3.21–3.26 (m, 1H), 3.03 (dd, J=2.8, 10.6 Hz, 1H), 2.10 (s, 6H), 1.47–1.55 (m, 2H), 0.98–1.01 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 132.1, 132.0, 127.3, 127.0, 117.1, 117.0, 52.8, 47.4, 27.8, 19.6, 10.8; HRMS (ESI) calcd for $C_{12}H_{19}N_2$ $[M+H]^+$: 191.1543, found: 191.1552.

*4.4.9. 1,2,3,4-Tetrahydroquinoxaline(**2i**)*[11a]. Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58–6.61 (m, 2H), 6.48–6.52 (m, 2H), 3.63 (br, 2H), 3.42 (s, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.5, 119.5, 115.5, 42.2; HRMS (ESI) calcd for $C_8H_{11}N_2$ $[M+H]^+$: 135.0917, found: 135.0922.

*4.4.10. 2,3-Dimethyl-1,2,3,4-tetrahydroquinoxaline (**2j**).* Yellow solid, mp 113–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65–6.67 (m, 2H), 6.54–6.56 (m, 2H), 3.62 (br, 2H), 3.50–3.54 (m, 2H), 1.16 (s, J=6.0 Hz, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 133.4, 119.2, 115.1, 49.7, 18.0; HRMS (ESI) calcd for $C_{10}H_{15}N_2$ $[M+H]^+$: 163.1230, found: 163.1236.

*4.4.11. 2-Phenyltetrahydroquinoxaline (**2k**)*[5g,h,j,19]. Yellow solid, mp 121–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.41 (m, 5H), 6.58–6.67 (m, 4H), 4.48 (dd, J=5.2, 8.1 Hz, 1H), 3.84 (br, 2H), 3.46 (dd, J=8.1, 11.1 Hz, 1H), 3.33 (dd, J=5.4, 8.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 142.6, 134.9, 133.6, 129.4, 128.7, 127.8, 119.7, 119.6, 115.5, 115.2, 55.5, 49.9; HRMS (ESI) calcd for $C_{14}H_{15}N_2$ $[M+H]^+$: 211.1230, found: 211.1233.

*4.4.12. 2-(4-Fluorophenyl)-1,2,3,4-tetrahydroquinoxaline(**2l**).* Yellow solid, mp 94–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.37 (m, 2H), 7.03–7.08 (m, 2H), 6.63–6.66 (m, 2H), 6.57–6.60 (m, 2H), 4.48 (dd, J=2.9, 8.0 Hz, 1H), 3.82 (br, 2H), 3.43 (dd, J=3.0, 11.0 Hz, 1H), 3.29 (dd, J=2.84, 11.27 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 138.6, 134.9, 133.7, 129.6, 129.5, 119.9, 116.5, 116.3, 115.7, 115.4, 55.0, 50.1; HRMS (ESI) calcd for $C_{14}H_{14}N_2F$ $[M+H]^+$: 229.1136, found: 229.1141.

*4.4.13. 2-(4-Chlorophenyl)-1,2,3,4-tetrahydroquinoxaline(**2m**)*[5j]. Yellow solid, mp 104–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.36 (m, 4H), 6.63–6.67 (m, 2H), 6.56–6.60 (m, 2H), 4.47 (dd, J=3.0, 7.9 Hz, 1H), 3.82 (br, 2H), 3.43 (dd, J=3.1, 11.0 Hz, 1H), 3.28 (dd, J=8.0, 11.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.4, 134.7, 134.5, 133.7, 129.7, 129.3, 120.0, 119.9, 115.7, 115.5, 55.0, 49.9; HRMS (ESI) calcd for $C_{14}H_{14}N_2Cl$ $[M+H]^+$: 245.0840, found: 245.0845.

*4.4.14. 2-(4-Bromophenyl)-1,2,3,4-tetrahydroquinoxaline(**2n**)*[19]. Yellow solid, mp 144–146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.50 (m, 2H), 7.25–7.28 (m, 2H), 6.63–6.66 (m, 2H), 6.57–6.60 (m, 2H), 4.45 (dd, J=3.0, 7.9 Hz, 1H), 3.85 (br, 2H), 3.43 (dd, J=3.1, 11.0 Hz, 1H), 3.27 (dd, J=4.0, 11.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.9, 134.7, 133.7, 132.7, 129.6, 122.6, 120.0, 119.9, 115.7, 115.5, 55.1, 49.9; HRMS (ESI) calcd for $C_{14}H_{14}N_2Br$ $[M+H]^+$: 289.0335, found: 289.0339.

*4.4.15. 2-(4-Methoxyphenyl)-1,2,3,4-tetrahydroquinoxaline(**2o**)*[5j,19]. Yellow solid, mp 63–66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.33

(m, 2H), 6.91–6.93 (m, 2H), 6.64–6.66 (m, 2H), 6.57–6.59 (m, 2H), 4.43 (dd, *J*=3.0, 8.4 Hz, 1H), 3.83 (s, 3H), 3.81 (br, 2H), 3.42 (dd, *J*=3.1, 11.0 Hz, 1H), 3.31 (dd, *J*=8.3, 11.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 160.2, 135.1, 134.8, 133.8, 129.0, 119.7, 119.6, 115.5, 115.3, 114.9, 56.2, 55.0, 50.2; HRMS (ESI) calcd for $C_{15}H_{17}N_2O[M+H]^+$: 241.1335, found: 241.1339.

*4.4.16. 2-(2-Methoxyphenyl)-tetrahydroquinoxaline (**2p**)*[5g]. Yellow solid, mp 124–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.44 (m, 1H), 7.27–7.30 (m, 1H), 6.89–6.99 (m, 2H), 6.56–6.66 (m, 4H), 4.92 (dd, *J*=2.8, 7.0 Hz, 1H), 3.83 (br, 2H), 3.86 (s, 3H), 3.55 (dd, *J*=3.0, 10.9 Hz, 1H), 3.29 (dd, *J*=7.1, 11.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.3, 135.2, 133.8, 130.9, 129.2, 127.8, 121.6, 119.7, 119.3, 115.6, 115.3, 111.0, 56.1, 48.6, 47.5; HRMS (ESI) calcd for $C_{15}H_{17}N_2O$ $[M+H]^+$: 241.1335, found: 241.1338.

*4.4.17. 2-p-Tolyl-1,2,3,4-tetrahydroquinoxaline(**2q**)*[5j]. Yellow solid, mp 98–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.29 (m, 2H), 7.18–7.20 (m, 2H), 6.62–6.65 (m, 2H), 6.56–6.59 (m, 2H), 4.45 (dd, *J*=2.3, 8.0 Hz, 1H), 3.82 (br, 2H), 3.44 (dd, *J*=2.8, 11.0 Hz, 1H), 3.29–3.34 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 139.8, 138.6, 135.2, 133.8, 130.3, 127.9, 119.9, 119.7, 115.7, 115.4, 55.4, 50.2, 22.1; HRMS (ESI) calcd for $C_{15}H_{17}N_2[M+H]^+$: 225.1386, found: 225.1391.

*4.4.18. 2-(Biphenyl-4-yl)-1,2,3,4-tetrahydroquinoxaline(**2r**).* Yellow solid, mp 184–186 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.60 (m, 4H), 7.44–7.48 (m, 4H), 7.34–7.38 (m, 1H), 6.65–6.68 (m, 2H), 6.60–6.66 (m, 2H), 4.54 (dd, *J*=2.9, 8.0 Hz, 1H), 3.90 (br, 2H), 3.51 (dd, *J*=3.0, 11.0 Hz, 1H), 3.37 (dd, *J*=8.0, 11.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.9, 141.8, 141.7, 135.0, 133.8, 130.0, 128.4, 128.3, 128.1, 127.8, 120.0, 119.8, 115.7, 115.4, 55.4, 50.0; HRMS (ESI) calcd for $C_{20}H_{19}N_2[M+H]^+$: 287.1543, found: 287.1549.

*4.4.19. 2-Styryltetrahydroquinoxaline (**2s**)*[5g]. Yellow solid, mp 110–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.41 (m, 5H), 6.55–6.69 (m, 5H), 6.26 (dd, *J*=8.4, 15.9 Hz, 1H), 4.09–4.14 (m, 1H), 3.71 (br, 2H), 3.42 (dd, *J*=3.0, 10.8 Hz, 1H), 3.23 (dd, *J*=7.5, 10.8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 137.3, 133.9, 133.8, 132.4, 130.0, 129.4, 128.6, 127.3, 119.8, 119.6, 115.4, 115.4, 53.6, 47.6; HRMS (ESI) calcd for $C_{16}H_{17}N_2$ $[M+H]^+$: 237.1386, found: 237.1391.

*4.4.20. 2-(2′-Chloro-styryl)tetrahydroquinoxaline(**2t**)*[5g]. Yellow solid, mp 118–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J*=7.4 Hz, 1H), 7.35 (d, *J*=1.7 Hz, 1H), 7.20–7.22 (m, 2H), 7.06 (d, *J*=15.8, 1H), 6.55–6.64 (m, 4H), 6.27 (dd, *J*=8.2, 15.9 Hz, 1H), 4.14–4.19 (m, 1H), 3.61 (br, 2H), 3.51 (dd, *J*=2.9, 10.9 Hz, 1H), 3.31 (dd, *J*=7.2, 10.8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 135.4, 133.9, 133.7, 133.6, 132.9, 130.5, 129.6, 128.5, 127.7, 127.6, 119.8, 119.7, 115.4, 115.3, 53.6, 47.5; HRMS (ESI) calcd for $C_{16}H_{16}ClN_2$ $[M+H]^+$: 271.0997, found: 271.1000.

*4.4.21. 2-(3′-Nitro-styryl)tetrahydroquinoxaline(**2u**)*[5g]. Red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23–8.24 (m, 1H), 8.07–8.10 (m, 1H), 7.68 (d, *J*=7.7 Hz, 1H), 7.46–7.50 (m, 1H), 6.61 (d, *J*=15.9 Hz, 1H), 6.63–6.65 (m, 2H), 6.55–6.58 (m, 2H), 6.45 (dd, *J*=8.8, 15.9 Hz, 1H), 4.16–4.18 (m, 1H), 3.76 (br, 2H), 3.51 (dd, *J*=3.1, 10.9 Hz, 1H), 3.29 (dd, *J*=6.7, 11.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 149.3, 139.2, 133.7, 133.6, 133.5, 133.1, 130.3, 129.9, 123.0, 121.8, 119.8, 119.6, 115.5, 115.3, 53.3, 47.2; HRMS (ESI) calcd for $C_{16}H_{16}N_3O_2$ $[M+H]^+$: 282.1237, found: 282.1244.

4.5. General procedure for asymmetric transfer hydrogenation of quinoxalines

A carousel reaction tube containing a magnetic stirring bar and metal precursor (2.5 μmol), ligand **3h** (2.5 mg, 6 μmol), quinoxaline substrate (0.5 mmol), and HCOONa (340 mg, 5 mmol) in an aqueous solution of HOAc/NaOAc (5 M, 5 mL, pH=5.5 or pH=4.3 with 0.3 mL EtOAc) was sealed without degassing. The reaction mixture was stirred at 40 °C for the time indicated, then cooled to room temperature and basified with an aqueous solution of KOH. The resulting mixture was extracted with diethyl ether (3×5 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the product was purified by flash column chromatography. The ee was determined by HPLC with an OD-H chiral column.

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