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FACILE FORMATION OF IMIDAZOLINIUM SALT BY REACTION OF CORRESPONDING DIAMINE AND TRIMETHYL ORTHOFORMATE IN 1,1,1,3,3,3-HEXAFLUOROISOPROPANOL

Kensuke Usui and Masahisa Nakada*

Department of Chemistry and Biochemistry, School of Advanced Science and Engineering, Waseda University, 3-4-1 Ohkubo, Shinjuku-ku, Tokyo 169-8555, Japan; E-mail: mnakada@waseda.jp

Dedicated to Professor Victor Snieckus on the occasion of his 77th birthday

Abstract – The preparation of imidazolinium salts, which can be used as precursors of pincer-type *N*-heterocyclic carbene ligands, is described. The formation of imidazolinium salts under standard conditions is difficult, but they have been successfully synthesized by reaction of the corresponding diamines and trimethyl orthoformate in 1,1,1,3,3,3-hexafluoroisopropanol. The synthesis of new chiral C_2 symmetric imidazolinium salts is also described.

N-Heterocyclic carbenes (NHCs) were first reported as organometallic complexes by Öfele[1] and Wanzlick,[2] and were isolated as stable crystals by Arduengo[3] in 1968. Since their discovery, stable NHCs have been drawing attraction from many chemists because of their unique structures and properties. NHCs have been extensively studied, especially in oganometallic chemistry, as new ligands that can be used as substitutes for phosphine ligand.[4] Recently, NHCs have also been recognized as organocatalysts.[5] Research on NHCs is therefore expected to be further developed.

Pincer-type ligands have been studied since the early 1970s, and are known to form stable metal complexes[6] by forming carbon–metal bonds and coordination bonds with σ-donor heteroatoms such as nitrogen and phosphorus. Metal complexes of pincer-type ligands show high and long-lasting catalytic activities, and have therefore been used for many catalytic reactions.

Consequently, pincer-type NHC ligands are expected to be useful. However, a limited number of pincer-type NHC ligands have been described,[7,8] and their applications in asymmetric catalysis have not been reported. The development of new pincer-type NHC ligands could contribute to developments in organometallic chemistry as well as asymmetric catalysis.

We therefore decided to design and synthesize chiral C_2 symmetric pincer-type NHC ligands **1** and **2**, which are shown as their complexes in Figure 1. In this paper, we report the preparation of imidazolinium salts corresponding to **1** and **2**, which are only formed in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP).

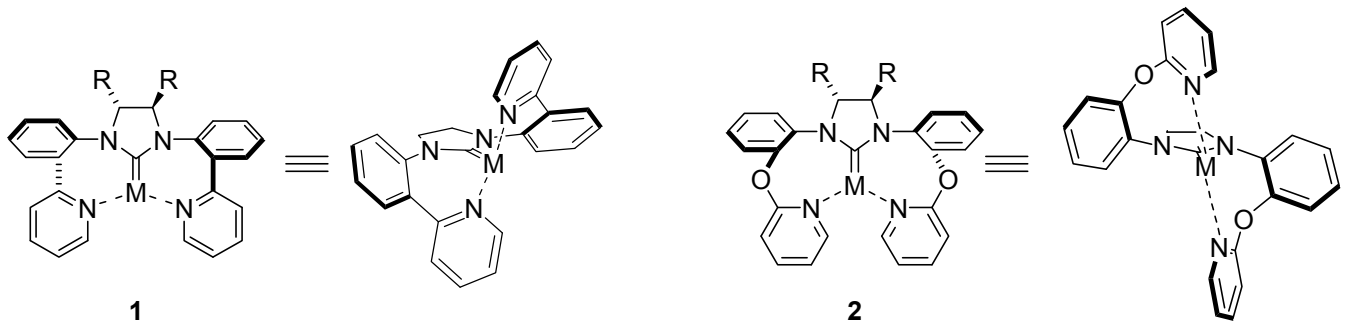
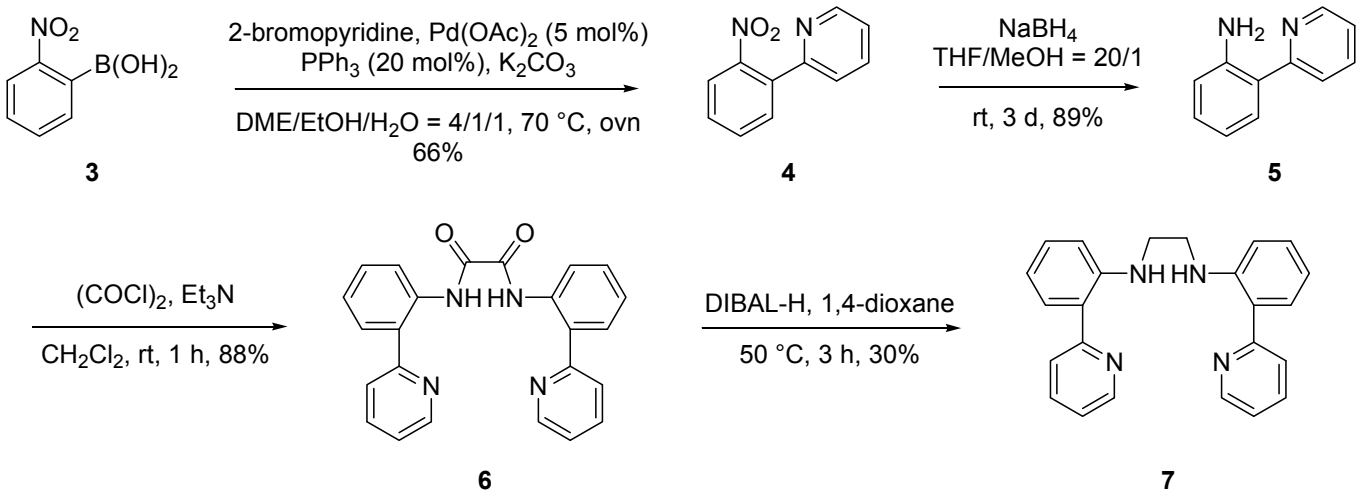


Figure 1. Designed pincer-type NHC ligands

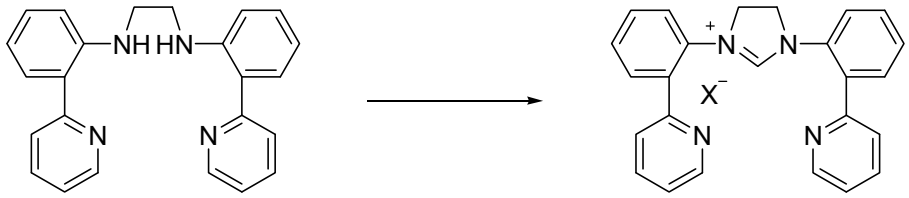
We first prepared achiral diamine **7** (Scheme 1) to investigate the preparation and properties of the corresponding imidazolinium salts and NHCs. The first step in the synthesis of **7** was the preparation of **4** by a Suzuki–Miyaura coupling reaction. The palladium-catalyzed coupling reaction of *o*-nitrophenylboronic acid **3**, which was prepared from 1-iodo-2-nitrobenzene according to the report by Yu,[9] with 2-bromopyridine afforded **4** under standard conditions. Reduction of **4** with $NaBH_4$ gave arylamine **5**, which was converted to bis-amide **6** by reaction with oxallyl chloride; subsequent DIBAL-H reduction afforded diamine **7**.



Scheme 1. Preparation of diamine **7**

We next examined the conversion of diamine **7** to the corresponding imidazolinium salts (Table 1). However, none of the reactions using the reported conditions afforded imidazolinium salts **8** (entries 1–4). The low reactivity of diamine **7** was assumed to be the result of internal hydrogen bonding of the 1,2-diamine. The reaction was therefore carried out in 1-butanol to weaken the hydrogen bonds (entry 4). As a result, a polar compound was formed, which appeared on the base line in thin-layer chromatography, but was converted to the formamide of **7** during evaporation of the solvent. HFIP is a volatile solvent and easily removed under reduced pressure. Moreover, HFIP has been reported to be slightly acidic (p*K*a = 9.3) and a strong hydrogen-bond donor with high ionizing power and polarity; it therefore activates orthoesters towards nucleophilic attack of amino groups.[10] So, we examined the reaction of **7** with trimethyl orthoformate in HFIP, and found that the reaction proceeded even at room temperature (entry 5) to afford imidazolinium salts **8a** and **8b** in79% and 73% yields, respectively.

Table 1. Preparation of imidazolinium salts **8a** (**X** = BF_4) and **8b** (**X** = Cl)

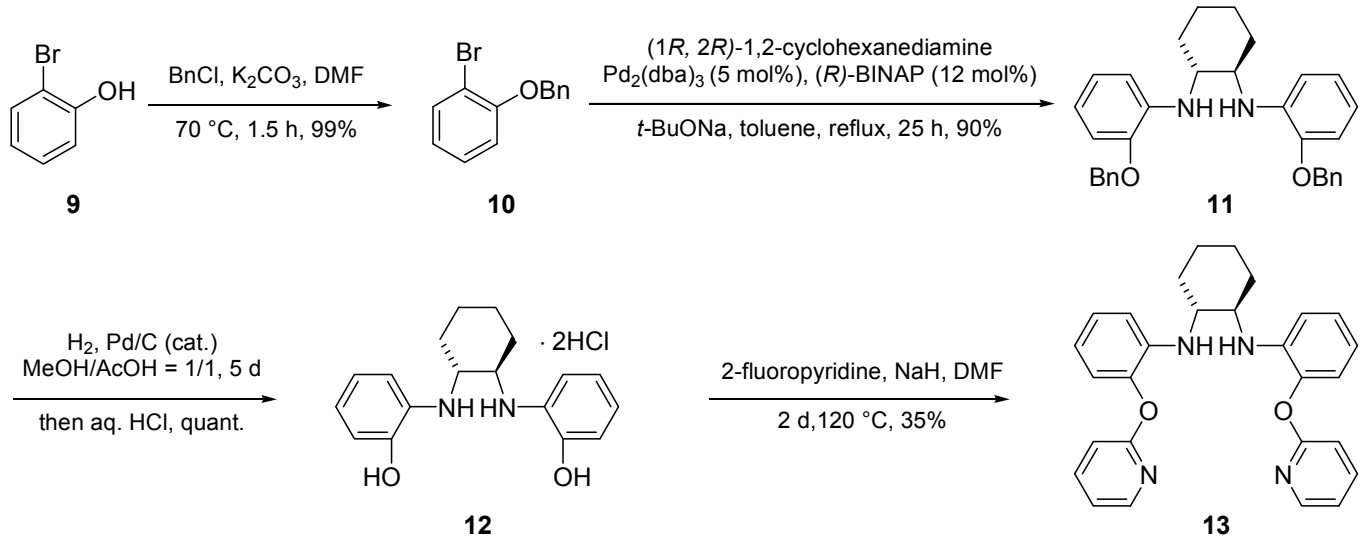


7 **8**

entry	reagent (equiv)	solvent	temp (°C)	yield (%)[a]
1	NH_4BF_4 (3.0), HCO_2H (cat.),	$HC(OEt)_3$	120	0
2	NH_4BF_4 (3.0)	$HC(OEt)_3$/toluene = 1/10	reflux	0
3	NH_4BF_4 (3.0), $HC(OEt)_3$ (2.0)	toluene	reflux	0
4	NH_4BF_4 (3.0)	$HC(OEt)_3$/*n*-BuOH = 1/10	reflux	0
5	NH_4BF_4 (1.2)	HC $(OMe)_3$/HFIP = 1/10	rt	79 (**X** = BF_4)
6	NH_4Cl (1.2)	$HC(OMe)_3$/HFIP = 1/10	rt	73 (**X** = Cl)

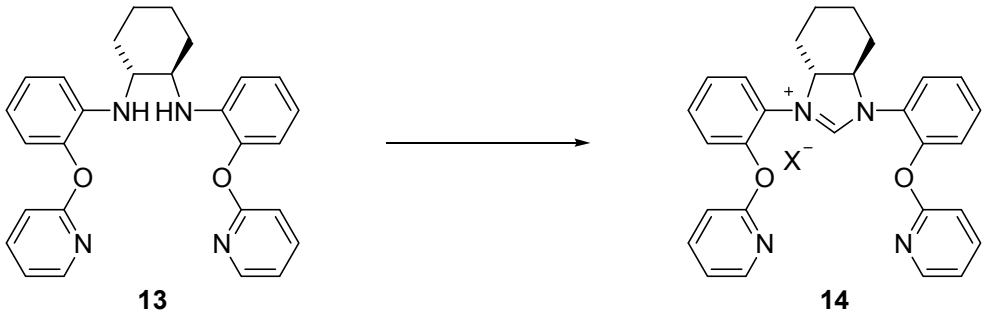
[a]Yields determined by ^{1}H-NMR using fluorene as internal standard.

Once imidazolinium salts **8a** and **8b** had been successfully synthesized, we proceeded to prepare chiral diamine **13** and its imidazolinium salts. 2-Bromophenyl benzyl ether **10**, prepared from 2-bromophenol **9**, was converted to compound **11** by a palladium-catalyzed coupling reaction. Benzyl ethers in **11** were removed by hydrogenolysis to afford bisphenol **12**, which was successfully converted to the chiral diamine **13** by reaction with 2-fluoropyridine.



Scheme 2. Preparation of diamine **13**

Table 2. Preparation of imidazolinium salts **14a** (**X** = BF_4) and **14b** (**X** = Cl)



entry	reagent (equiv)	solvent	temp (°C)	yield (%)[a]
1	NH_4BF_4 (5.0)	$HC(OEt)_3$	120	0
2	NH_4Cl (5.0)	$HC(OEt)_3$	120	0
3	HCl, EtOH	$HC(OEt)_3$	120	0
4	NH_4BF_4 (1.2)	$HC(OMe)_3$/HFIP = 1/10	rt	59 (**X** = BF_4)
5	NH_4Cl (1.2)	$HC(OMe)_3$/HFIP = 1/10	rt	73 (**X** = Cl)

[a]Yields determined by ^{1}H-NMR using fluorene as internal standard.

Diamine **13** was not converted to the corresponding imidazolinium salts under standard conditions (Table 2, entries 1-3); however, the reaction conditions used for the synthesis of **8** (Table 1, entries 5 and 6) significantly accelerated the formation of imidazolinium salts **13**, even at room temperature, and **13a**

(entry 5) and **13b** (entry 6) were successfully obtained in 59% and 73% yields, respectively.

Imidazolinium salts **8** and **14** were unstable and easily hydrolyzed and converted to the corresponding formamides. The formation of these salts was therefore confirmed by ^{1}H-NMR spectroscopy and mass spectrometry of the crude products. Selected chemical shifts [δ (ppm), downfield from tetramethylsilane] of imidazolinium salts **8** and **14** are shown in Figure 2.

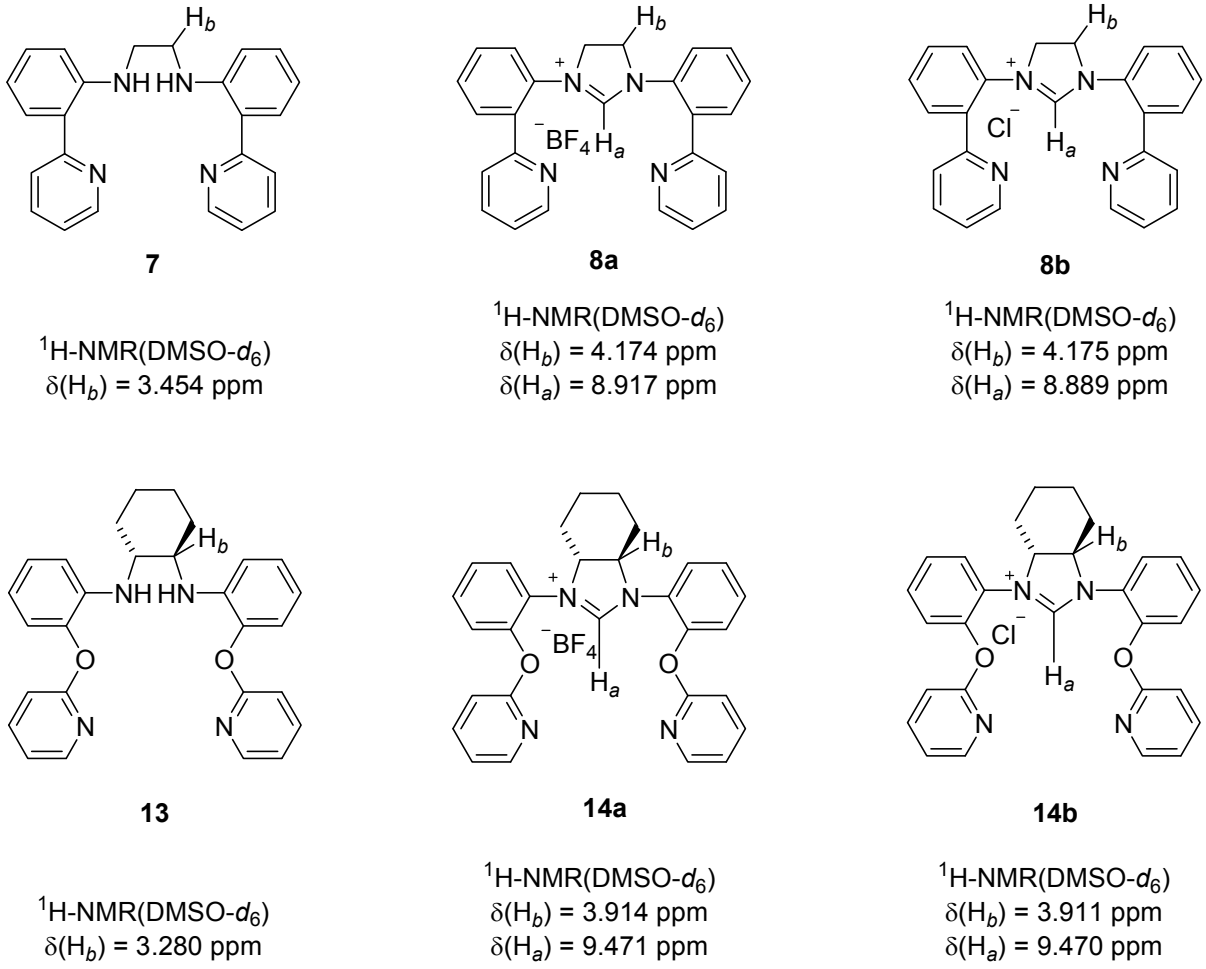


Figure 2. Selected chemical shifts [δ (ppm), downfield from tetramethylsilane] of diamines **7** and **13**, and imidazolinium salts **8** and **14**

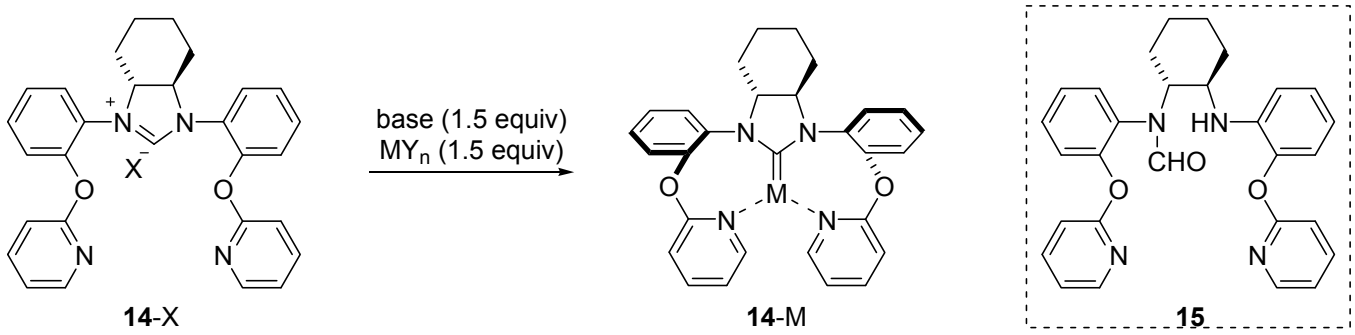
Imidazolinium salts **8** and **14** were found to be unstable in less-polar solvents, but, interestingly, were stable in polar solvents such as methanol and dimethyl sulfoxide (DMSO). For all the imidazolinium salts, the H_b signals were found at around 4 ppm (downfield from tetramethylsilane) in DMSO-d_6, i.e., shifted downfield compared with the H_b signals of the corresponding diamines, and the H_a signals appeared at around 9 ppm, suggesting formation of the imidazolinium salts.

Once imidazolinium salts **14a** and **14b** were obtained as described above, we finally examined the synthesis of metal complexes of **14**-M (Table 3). As the imidazolinium salts **14a** and **14b** were unstable, they were prepared just before the reactions in Table 3, and used after removing all volatile materials under reduced pressure.

We first examined the synthesis of silver complexes of **14a** and **14b**, which have been reported to be converted to various metal complexes.[11] The reactions of **14a** and **14b** with Ag_2O were carried out in the presence of MS 4A, but complex mixtures or only formamide **15** were obtained (entries 1–3).

We then examined the synthesis of palladium complexes of **14a** and **14b** using a base and $Pd(OAc)_2$, but only observed the formation of complex mixtures (entries 4–6). The formation of **15** suggests that it might be derived from the NHC of **14b**, which is too unstable to be isolated. Usually, imidazolinium salts are stable and isolable in air. The low stability of the NHC of **14** could therefore be attributed to a factor such as degradation accelerated via ylide formation by the formed carbene and pyridine nitrogen. The unsuccessful results in Table 3 will be useful in the further design and synthesis of new NHC ligands.

Table 3. Attempted preparation of metal complexes of **14a** and **14b**



entry	X	base	M_xY_z	solvent	temp (°C)	yield (%)
1[a]	Cl	none	Ag_2O[b]	$(CH_2Cl)_2$	rt	complex mixture
2[a]	Cl	none	Ag_2O[b]	$(CH_2Cl)_2$	80	0[c]
3[a]	BF_4	none	Ag_2O[b]	$(CH_2Cl)_2$	rt	complex mixture
4	BF_4	NaOMe	$Pd(OAc)_2$	MeOH	rt	complex mixture
5	BF_4	KHMDS	$Pd(OAc)_2$	THF	rt	complex mixture
6	BF_4	*t*-BuOK	$Pd(OAc)_2$	THF	rt	complex mixture

[a]MS 4A was added. [b]1.0 equiv Ag_2O was used. [c]Formamide **15** was formed.

In conclusion, new chiral C_2 symmetric imidazolinium salts were successfully synthesized. We found that the formation of imidazolinium salts was significantly enhanced, even at room temperature, when the reaction was carried out in HFIP. The use of HFIP in the synthesis of imidazolinium salts enables the formation of new imidazolinium salts that are difficult to prepare under known conditions. Further investigations of the use of HFIP in the preparation of imidazolinium salts are now underway, and the results will be reported in due course.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on 400 MHz spectrometer. ^{1}H and ^{13}C chemical shifts are reported in ppm downfield from tetramethylsilane (TMS, δ scale) with the solvent resonances as internal standards. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; band, several overlapping signals; brs, broad. IR spectra were recorded on a FT/IR spectrometer. Mass spectra were provided at the Materials Characterization Central Laboratory, Waseda University. All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica gel plates using UV light as visualizing agent and phosphomolybdic acid and heat as developing agents. Silica gel (60, particle size 0.040-0.063 mm) was used for flash chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on self-made 0.3 mm silica gel plates. THF was distilled from sodium/benzophenone ketyl. Toluene was distilled from sodium. MeOH was distilled with a small amount of magnesium and I_2. All commercially available reagents were used without further purification. Optical rotations were measured on a polarimeterat a wavelength of 589 nm. High resolution mass spectra (HRMS) were obtained by either an electronspray ionization (ESI) or a fast atom bombardment (FAB), and theoretical monoisotopic molecular masses were typically ≤5 ppm. Melting point was uncorrected. Melting point was uncorrected. TLC Rfs of purified compounds were included.

2-(2-Nitrophenyl)pyridine (4).[12] To a suspension of K_2CO_3 (4.65 g, 33.6 mmol), $Pd(OAc)_2$ (0.189 g, 0.840 mmol), and PPh_3 (0.882 g, 3.36 mmol) in 170 mL of DME/EtOH/H_2O = 4/1/1 was added 2-nitrophenylboronic acid (**3**) (3.37 g, 20.2 mmol) and 2-bromopyridine (1.60 mL, 16.8 mmol). After stirring at 70 °C overnight, the reaction mixture was concentrated under reduced pressure. To the residue were added water (100 mL) and Et_2O (100 mL), and the aqueous layer was extracted with Et_2O (50 mL × 2). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, and evaporated. The residue was purified by silica gel chromatography (hexane/EtOAc = 6/1) to afford 2-(2-nitrophenyl)pyridine (**4**) (2.23 g, 66%) as white solid. Spectroscopic data were in agreement with those previously reported:[12] R_f = 0.28 (hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, J =

5.0 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.81 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.63 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.55 (dd, *J* = 7.7, 7.2 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.32 (dd, *J* = 7.7, 5.0 Hz, 1H).

2-(Pyridin-2-yl)benzenamine (**5**).[13] To a solution of 2-(2-nitrophenyl)pyridine (**4**) (2.23 g, 11.1 mmol) in THF/ MeOH = 20/1 (230 mL) was added $NaBH_4$ (2.53 g, 66.9 mmol). After stirring at room temperature for 3 days, the reaction mixture was concentrated under reduced pressure. To the residue were added water (100 mL) and Et_2O (100 mL), and the aqueous layer was extracted with Et_2O (50 mL × 2). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, and evaporated. The residue was purified by silica gel chromatography (hexane/EtOAc = 10/1) to afford 2-(pyridin-2-yl)benzeneamine (**5**) (1.68 g, 89%) as a reddish liquid. Spectroscopic data were in agreement with those previously reported:[13] R_f = 0.43 (hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, *J* = 5.0 Hz, 1H), 7.77 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.21–7.15 (m, 2H), 6.79 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.77 (d, *J* = 7.7 Hz, 1H), 5.74 (br, 2H).

***N*^{1},*N*^{2}-Bis(2-(pyridin-2-yl)phenyl)oxalamide** (**6**). To a solution of 2-(pyridin-2-yl)benzeneamine (**5**) (1.68 g, 9.89 mmol) and Et_3N (1.67 mL, 11.9 mmol) in dichloromethane (DCM) (50 mL) was added a solution of $(COCl)_2$ (ca. 0.5 mL) in DCM (2 mL) dropwise at room temperature until the starting material disappeared. The resulting mixture was quenched with saturated aqueous $NaHCO_3$ (20 mL), and the aqueous layer was extracted with DCM (20 mL × 2). The combined organic layers were washed with water (20 mL), dried over Na_2SO_4, and evaporated. The residue was purified by trituration (hexane/EtOAc = 2/1) to afford *N*^{1},*N*^{2}-*bis*(2-(pyridin-2-yl)phenyl)oxalamide (**6**) (1.71 g, 88%) as a reddish brown solid: R_f = 0.41 (hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.68 (s, 2H), 8.88 (d, *J* = 4.9 Hz, 2H), 8.67 (d, *J* = 8.3 Hz, 2H), 7.84 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.72 (d, *J* = 7.8 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.47 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.31 (dd, *J* = 7.8, 4.9 Hz, 2H), 7.25 (dd, *J* = 8.3, 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 157.5, 148.3, 137.6, 136.3, 129.9, 128.9, 127.3, 124.5, 122.6, 122.1, 121.8; IR (ATR): 3059.2, 1678.4, 1583.6, 1512.0, 1474.1, 1439.3, 1419.7, 1312.5, 753.6, 547.9 cm^{-1}; mp 225 °C; HRMS (ESI) calcd. for $C_{24}H_{19}O_2N_4$ [M+H$^+$] 395.1503, found 395.1502.

***N*^{1},*N*^{2}-Bis(2-(pyridin-2-yl)phenyl)ethylenediamine (7).** To a solution of *N*^{1},*N*^{2}-bis(2-(pyridin-2-yl)phenyl)oxalamide (**6**) (105 mg, 0.266 mmol) in 1,4-dioxane (2.7 mL) was added DIBAL (1.02 M in toluene, 2.22 mL, 2.26 mmol). After stirring at 50 °C for 3 h, the resulting mixture was quenched with saturated aqueous Rochelle salt (3 mL) and diluted with Et_2O (5 mL), and the aqueous layer was extracted with Et_2O (5 mL × 2). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by silica gel chromatography (hexane/EtOAc = 15/1) to afford *N*^{1},*N*^{2}-bis(2-(pyridin-2-yl)phenyl)ethylenediamine (**7**) (29.0 mg, 30%) as a yellow solid: R_f = 0.50 (hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (br, 2H), 8.30 (d, *J* = 5.0 Hz, 2H), 7.70 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.26 (dd, *J* = 8.2, 7.2 Hz, 2H),

7.07 (dd, *J* = 7.2, 5.0 Hz, 2H), 6.83 (d, *J* = 7.7 Hz, 2H), 6.73 (dd, *J* = 7.7, 7.7 Hz, 2H), 3.55 (s, 4H); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.62 (br, 2H), 8.23 (d, *J* = 5.0 Hz, 2H), 7.85 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 2H), 7.23 (dd, *J* = 8.2, 7.7 Hz, 2H), 7.21 (dd, *J* = 7.7, 5.0 Hz, 2H), 6.82 (d, *J* = 7.7 Hz, 2H), 6.67 (dd, *J* = 7.7, 7.7 Hz, 2H), 3.46 (br, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 147.6, 147.3, 136.7, 130.3, 129.4, 122.1, 121.6, 120.6, 115.8, 111.4, 42.6; IR (ATR): 3257.7, 3056.6, 2849.0, 1602.7, 1580.9, 1560.6, 1510.2, 1477.0, 1439.0, 744.2, 626.3 cm^{-1}; mp 146.4 °C; HRMS (ESI) calcd. for $C_{24}H_{23}N_4$ [M+H$^+$] 367.1917, found 367.1917.

General procedure for the preparation of imidazolinium salts. To a suspension of diamine and NH_4X (1.2 equiv. of diamine) in HFIP (0.1 M) was added $CH(OMe)_3$ (10% w/w of HFIP). After stirring at room temperature for 1 h, to the mixture was added an internal standard, and then the excess $CH(OMe)_3$ and HFIP were removed under reduced pressure to afford a crude residue. The residue was dissolved in DMSO-d_6, and the solution was analyzed by ^{1}H-NMR. NMR yields were obtained by careful integration based on the internal standard.

1,3-Bis(2-(pyridin-2-yl)phenyl)imidazolinium tetrafluoroborate (**8a**). According to general procedure, 1,3-bis(2-(pyridin-2-yl)phenyl)imidazolinium tetrafluoroborate (**8a**) was prepared from *N*^{1},*N*^{2}-bis(2-(pyridin-2-yl)phenyl)ethylenediamine (**7**) (8.0 mg, 0.022 mmol) and NH_4BF_4 (2.7 mg, 0.026 mmol). The NMR yield was obtained using fluorene (3.9 mg, 0.024 mmol) as an internal standard (79%): R_f = 0.25 (DCM/MeOH = 10/1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.92 (s, 1H), 8.71 (d, *J* = 4.6 Hz, 2H), 8.00 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.78–7.74 (m, 2H), 7.72 (d, *J* = 7.8 Hz, 2H), 7.66–7.60 (m, 6H), 7.50 (dd, *J* = 7.8, 4.6 Hz, 2H), 4.17 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.9, 157.2, 155.0, 149.5, 137.7, 136.0, 133.7, 131.2, 130.0, 127.3, 124.0, 123.2, 52.7; HRMS (ESI) calcd. for $C_{25}H_{21}N_4$ [M-BF_4^-] 377.1761, found 377.1754.

1,3-Bis(2-(pyridin-2-yl)phenyl)imidazolinium chloride (**8b**). According to general procedure, 1,3-bis(2-(pyridin-2-yl)phenyl)imidazolinium chloride (**8b**) was prepared from *N*^{1},*N*^{2}-bis(2-(pyridin-2-yl)phenyl)ethylenediamine (**7**) (9.1 mg, 0.025 mmol) and NH_4Cl (1.6 mg, 0.030 mmol). The NMR yield was obtained using fluorene (5.2 mg, 0.031 mmol) as an internal standard (73%): R_f = 0.14 (DCM/MeOH = 10/1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.89 (s, 1H), 8.68 (d, *J* = 5.0 Hz, 2H), 7.98 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.75–7.72 (m, 2H), 7.70 (d, *J* = 7.7 Hz, 2H), 7.65–7.59 (m, 6H), 7.48 (dd, *J* = 7.7, 5.0 Hz, 2H), 4.18 (s, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-*d*6): δ 158.9, 157.3, 155.0, 149.5, 137.7, 136.0, 133.7, 131.1, 130.0, 127.3, 124.0, 123.2, 52.7 ppm; HRMS (ESI): calcd. for $C_{25}H_{21}N_4$ [M-Cl^-] 377.1761, found 377.1761.

2-Benzyloxybromobenzene (**9**).[13] To a suspension of 2-bromophenol (**8**) (1.79 g, 10.4 mmol) and K_2CO_3 (2.86 g, 20.7 mmol) in DMF (10 mL) was added benzyl chloride (1.31 mL, 11.4 mmol). After stirring at 70 °C for 1.5 h, to the resulting mixture was added MeOH (0.5 mL), Et_2O (20 mL), and water (20 mL),

and the aqueous layer was extracted with Et_2O (10 mL × 2). The combined organic layers were washed with water (20 mL) and brine (20 mL), dried over Na_2SO_4, and evaporated. The residue was purified by silica gel chromatography (hexane/EtOAc = 100/1) to afford 2-benzyloxybromobenzene (**9**) (2.69 g, 99%) as a clear liquid. Spectroscopic data were in agreement with those previously reported:[13] R_f = 0.71 (hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.39 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.33 (d, *J* = 7.3 Hz, 1H), 7.23 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H) 5.17 (s, 2H).

(1*R*,2*R*)-*N*^{1},*N*^{2}-Bis(2-benzyloxyphenyl)-1,2-cyclohexanediamine (**10**). To a suspension of NaO^{t}Bu (980 mg, 10.2 mmol), (*R*)-BINAP (254 mg, 0.407 mmol), and $Pd_2(dba)_3$ (156 mg, 0.170 mmol) in degassed toluene (12 mL), was added a solution of (1*R*,2*R*)-1,2-cyclohexanediamine (388 mg, 3.40 mmol) and 2-benzyloxybromobenzene (**9**) (2.24 g, 8.48 mmol) in degassed toluene (5 mL). After stirring at 140 °C for 25 h, the resulting mixture was diluted with Et_2O (30 mL), filtered through a Celite® pad, and evaporated. The residue was purified by silica gel chromatography (hexane/EtOAc = 50/1) to afford (1*R*,2*R*)-*N*^{1},*N*^{2}-bis(2-benzyloxyphenyl)-1,2-cyclohexanediamine (**10**) (1.46 g, 90%) as a clear viscous liquid: R_f = 0.35 (hexane/EtOAc = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.12 (m, 10H), 6.88 (dd, *J* = 7.8, 7.8 Hz, 2H), 6.81 (d, *J* = 7.8 Hz, 2H), 6.71 (d, *J* = 7.8 Hz, 2H), 6.64 (dd, *J* = 7.8, 7.8 Hz, 2H), 4.99 (d, *J* = 12.0 Hz, 2H), 4.93 (d, *J* = 12.0 Hz, 2H), 4.57 (br, 2H), 3.30 (br, 2H), 2.31 (br, 2H), 1.75 (br, 2H), 1.43 (br, 2H), 1.31 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4, 138.4, 137.2, 128.4, 127.7, 127.1, 121.8, 116.3, 111.9, 110.5, 70.5, 57.0, 32.4, 24.5; IR (ATR): 3405.7, 3062.2, 2928.7, 2856.2, 1599.8, 1506.4, 1444.7, 1023.4, 732.0, 696.1 cm^{-1}; $[\alpha]_D^{27}$ +5.4 (*c* 0.0054, $CHCl_3$); HRMS (ESI) calcd. for $C_{32}H_{35}O_2N_2$ [M+H$^+$] 479.2693, found 479.2695.

(1*R*,2*R*)-*N*^{1},*N*^{2}-Bis(2-hydroxyphenyl)-1,2-cyclohexanediamine dihydrochloride (**11**). To a solution of (1*R*,2*R*)-*N*^{1},*N*^{2}-bis(2-benzyloxyphenyl)-1,2-cyclohexanediamine (**10**) (336 mg, 0.701 mmol) in MeOH/AcOH = 1/1 (8 mL) was added Pd/C (743 mg, 0.0701 mmol). After vigorously stirring under H_2 atmosphere at room temperature for 5 days, the resulting mixture was diluted with EtOAc (10 mL) and filtered through a Celite® pad. The filtrate was added conc. HCl (0.2 mL) and evaporated, and then the residue was purified by trituration (EtOAc) to afford (1*R*,2*R*)-*N*^{1},*N*^{2}-bis(2-hydroxyphenyl)-1,2-cyclohexanediamine dihydrochloride (**11**) (284 mg, quant.) as a gray powder: R_f (before hydrochloride salt) = 0.35 (hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.27 (br, 2H), 8.36 (br, 2H), 7.14 (d, *J* = 7.3 Hz, 2H), 6.95 (d, *J* = 7.3 Hz, 2H), 6.92 (dd, *J* = 7.3, 7.3 Hz, 2H), 6.80 (dd, *J* = 7.3, 7.3 Hz, 2H), 3.58 (br, 2H), 1.88 (br, 2H), 1.66 (br, 2H), 1.40 (br, 2H), 1.21 (br, 2H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 148.9, 127.3, 124.9, 120.4, 119.3, 115.7, 58.7, 28.5, 23.5; IR (ATR): 2941.7, 2680.2, 1736.7, 1600.4, 1508.6, 1470.6, 1236.5, 1097.8, 1039.9, 751.1 cm^{-1}; $[\alpha]_D^{29}$–16.0 (*c* 0.0050, MeOH); mp 111 °C (decomposition); HRMS (ESI) calcd. for $C_{18}H_{22}O_2N_2Na$ [M–2HCl+Na$^+$] 321.1573, found 321.1574.

(1*R*,2*R*)-N^1,N^2-Bis(2-(pyridin-2-yloxy)phenyl)-1,2-cyclohexanediamine (**12**). To a suspension of NaH (60% in oil, 132 mg, 3.29 mmol) in DMF (3.3 mL) was added (1*R*,2*R*)-N^1,N^2-bis(2-hydroxyphenyl)-1,2-cyclohexanediamine dihydrochloride (**11**) and 2-fluoropyridine (0.283 mL, 3.29 mmol). After stirring at 120 °C for 2 days, to the resulting mixture were added water (5 mL) and Et_2O (5 mL), and the aqueous layer was extracted with Et_2O (5 mL × 2). The combined organic layers were washed with water (10 mL) and brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by silica gel chromatography (hexane/EtOAc = 4/1) to afford (1*R*,2*R*)-N^1,N^2-bis(2-(pyridin-2-yloxy)phenyl)-1,2-cyclohexanediamine (**12**) (103 mg, 35%) as a clear viscous liquid: R_f = 0.35 (hexane/EtOAc = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 5.1 Hz, 2H), 7.51 (dd, *J* = 8.0, 7.0 Hz, 2H), 7.01 (dd, *J* = 8.0, 7.6 Hz, 2H), 6.93 (d, *J* = 7.6 Hz, 2H), 6.90 (dd, *J* = 7.0, 5.1 Hz, 2H), 6.71 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 6.34 (dd, *J* = 7.6, 7.6 Hz, 2H), 4.09 (br, 2H), 3.20 (br, 2H), 2.09 (br, 2H), 1.23 (br, 6H); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.06 (d, *J* = 4.9 Hz, 2H), 7.67 (dd, *J* = 8.2, 6.8 Hz, 2H), 7.01 (dd, *J* = 6.8, 4.9 Hz, 2H), 6.94 (dd, *J* = 7.7, 7.7 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 2H), 6.77 (d, *J* = 7.7 Hz, 2H), 6.75 (d, *J* = 7.7 Hz, 2H), 6.53 (dd, *J* = 7.7, 7.7 Hz, 2H), 4.54 (br, 2H), 3.28 (br, 2H), 1.92 (br, 2H), 1.58 (br, 2H), 1.18 (br, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 147.8, 141.1, 140.4, 139.3, 125.9, 121.5, 118.4, 116.7, 112.3, 110.4, 56.4, 31.7, 24.0; IR (ATR): 3394.8, 3056.8, 2930.3, 2855.7, 1606.3, 1509.7, 1466.3, 1424.5, 1234.9, 736.5 cm^{-1}; $[\alpha]_D^{28}$ +1.36 (*c* 0.012, $CHCl_3$); HRMS (ESI) calcd. for $C_{28}H_{28}O_2N_4Na$ [M+Na^+] 475.2104, found 475.2110.

(3a*R*,7a*R*)-1,3-Bis(2-(pyridin-2-yloxy)phenyl)-3a,4,5,6,7,7a-hexahydrobenzoimidazolium tetrafluoroborate (**14a**). According to general procedure, (3a*R*,7a*R*)-1,3-bis(2-(pyridin-2-yloxy)phenyl)-3a,4,5,6,7,7a-hexahydrobenzoimidazolium tetrafluoroborate (**14a**) was prepared from (1*R*,2*R*)-N^1,N^2-bis(2-(pyridin-2-yloxy)phenyl)-1,2-cyclohexanediamine (**12**) (13.1 mg, 0.029 mmol) and NH_4BF_4 (3.6 mg, 0.034 mmol). The NMR yield was obtained using phenanthrene (4.9 mg, 0.028 mmol) as an internal standard (59%): R_f = 0.28 (DCM/MeOH = 10/1); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.47 (s, 1H), 8.11 (d, *J* = 5.0 Hz, 2H), 7.84 (dd, *J* = 8.2, 6.9 Hz, 2H), 7.60 (d, *J* = 7.8 Hz, 2H), 7.55 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.42 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.17 (dd, *J* = 6.9, 5.0 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 3.92 (br, 2H), 2.06 (br, 2H), 1.76 (br, 2H), 1.42 (br, 2H), 1.19 (br, 2H); ^{13}C NMR (100 MHz, DMSO-*d*6): δ 161.7, 160.6, 148.2, 147.4, 140.8, 130.8, 126.9, 126.8, 125.8, 123.2, 120.1, 111.7, 69.5, 27.0, 23.1; HRMS (ESI) calcd. for $C_{29}H_{27}O_2N_4$ [M-BF_4^-] 463.2129, found 463.2129.

(3a*R*,7a*R*)-1,3-Bis(2-(pyridin-2-yloxy)phenyl)-3a,4,5,6,7,7a-hexahydrobenzoimidazolium chloride (**14b**). According to general procedure, (3a*R*,7a*R*)-1,3-bis(2-(pyridin-2-yloxy)phenyl)-3a,4,5,6,7,7a-hexahydrobenzoimidazolium chloride (**14**-Cl) was prepared from (1*R*,2*R*)-N^1,N^2-bis(2-(pyridin-2-yloxy)phenyl)-1,2-cyclohexanediamine (**12**) (13.4 mg, 0.030 mmol) and NH_4Cl (1.9 mg, 0.036 mmol). The NMR yield was obtained using phenanthrene (5.3 mg, 0.030 mmol) as an internal standard (73%): R_f

= 0.13 (DCM/MeOH = 10/1); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.47 (s, 1H), 8.08 (d, J = 5.4 Hz, 2H), 7.83 (dd, J = 8.6, 7.2 Hz, 2H), 7.61 (d, J = 8.2 Hz, 2H), 7.53 (dd, J = 8.2, 8.2 Hz, 2H), 7.41 (dd, J = 8.2, 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 7.15 (dd, J = 7.2, 5.4 Hz, 2H), 7.01 (d, J = 8.6 Hz, 2H), 3.91 (br, 2H), 2.04 (br, 2H), 1.74 (br, 2H), 1.40 (br, 2H), 1.18 (br, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.7, 160.6, 148.3, 147.4, 140.7, 130.8, 127.0, 126.9, 125.7, 123.1, 120.1, 111.7, 69.6, 27.0, 23.1; HRMS (ESI): calcd. for $C_{29}H_{27}O_2N_4$ [M-Cl$^-$] 463.2129, found 463.2131.

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