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Research Article

2-Oxiranyl-pyridines: Synthesis and Regioselective Epoxide Ring Openings with Chiral Amines as a Route to Chiral Ligands

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New epoxides, derivatives of pyridine, 2,2′-bipyridine, and 1,10-phenanthroline, were synthesized from the respective α-methylazaarenes. The obtained racemic 2-oxiranyl-azaarenes along with styrene oxide and trans-stilbene oxide were submitted to the ring opening with chiral primary amines as a chiral auxiliary. The most effective reaction was run in the presence of $Sc(OTf)_3$/diisopropylethylamine for 7 days at 80°C, affording a good yield of the amino alcohols. Except for styrene oxide which gave both α- and β-amino alcohols, the reactions led regioselectively to the corresponding diastereomeric β-amino alcohols. The resulting diastereomers were separated, and the configurations of their stereogenic centers were established. The obtained enantiomerically pure 2-pyridinyl- and 6-(2,2′-bipyridinyl)-β-amino alcohols were tentatively tested as chiral ligands in the zinc-catalyzed aldol reaction.

1. Introduction

Modular chiral ligands and catalysts attained in a few steps from the well-defined building blocks are considered as a useful tool for asymmetric synthesis [1–4]. Among functional blocks for the modular catalysts, the moieties of pyridine, 2,2′-bipyridine, and 1,10-phenanthroline, forming strong transition metal complexes, belong to the particularly promising ones [5–12]. For this aim, we intended to develop 2-oxiranyl-pyridines that, after epoxide ring openings, would give the desired chiral products.

For this purpose, we synthesize the 2-oxiranyl-azaarenes. Their epoxide ring-opening reactions with chiral amines should lead to the separable diastereomeric β-amino alcohols with the 2-pyridinyl-type substituents. Hence, obtained homochiral complexing amino alcohols would be tested as chiral ligands.

The key synthetic reaction will be carried out using the optimized regioselective epoxide ring opening with chiral primary amines as a chiral auxiliary. This approach has a literature precedent in the synthesis of individual enantiomers of 2-amino cyclohexanol derivatives using chiral 1-phenylethylamine at the epoxide ring-opening step followed by chromatographic separation of the diastereomeric alcohols [13]. Moreover, the method applied to our 2-oxiranyl-pyridines may offer a simple route to the chiral building blocks for important medicinal compounds [14, 15].

Generally, plentiful successful Lewis acid activators for the epoxide ring opening with amines have been developed [16–38]. The regiochemistry of the metal salt-catalyzed aminolysis of styrene oxide depends on the amine nucleophilicity and steric bulkiness as well as the strength of Lewis acid activator (metal ion) [39, 40]. Moreover, an interaction of the metal-ion additives with other complexing functionalities connected to the epoxide often influenced the observed regioselectivity [41–46]. Correspondingly, the metal-complexing pyridine-2-yl substituent demonstrated the regio-steering effect in the epoxide ring-opening reaction in the presence of $MgBr_2$ [9]. Although the asymmetric aminolysis of *meso*-epoxides was successful in the presence of chiral metal complexes [24–32], the respective racemic

trans-substituted epoxides could hardly be opened stereoselectively with other but aniline-type amine [23, 26].

2. Results and Discussion

2.1. Synthesis of 2-Oxiranyl-pyridines. In order to obtain the required α-azaarene epoxides (Scheme 1), we methylated the parent azaarenes, namely, 2,2′-bipyridine (bpy) and 1,10-phenanthroline (phen) with MeLi followed by the oxidative rearomatization [47, 48]. The α-methyl derivatives **1** (commercial), **2** [47], and **3** [48] were reacted with 1 equiv of benzaldehyde in the presence of a substoichiometric amount of calcium triflate [49]. The products, *trans*-styryl compounds **4** [50, 51], **5** and **6**, were formed in rather moderate yields. However, the unreacted methyl derivatives could be easily recovered. Moreover, when cyclohexyl carbaldehyde was used in the reaction with **3**, along with **6b** the diene **7** was obtained. Thus, in the next step, **4**, **5**, and **6** were reacted with NBS in dioxane/water acidified with acetic acid giving the respective bromohydrins **8**, **9**, and **10** that were smoothly converted into the epoxides **11** [52, 53, 54], **12**, and **13** (Scheme 1). Also, *rac*-2-(oxiranyl)pyridine (**14**) [55] was prepared analogously from 2-vinylpyridine.

2.2. Selective Epoxide Ring Opening: Model Studies. In order to find the proper conditions for our key reaction, the promising literature method for the $Sc(OTf)_3$-catalyzed epoxide ring opening [32, 39, 40] was examined. We run the model reaction of racemic epoxides, namely, styrene oxide (**15**) and *trans*-stilbene oxide (**16**) with chiral 1-phenylethylamine in the presence of $Sc(OTf)_3$/diisopropylethylamine (DIEA) at 80°C (Scheme 2).

The reaction of styrene oxide (**15**) with (*S*)-1-phenylethylamine gave both known regioisomers, β-amino alcohol **17** [56–58] and α-amino alcohol **18** [59], as a separable mixture (*ca.* 1 : 1), and their structures were confirmed by ^{1}H NMR spectroscopy [56–59]. Then, pure *like*-**17** and *unlike*-**17** diastereomers were separated by recrystallization (CH_2Cl_2/hexane). We ascribed their configurations by comparing the recorded ^{1}H NMR spectral properties and specific rotations with the reported ones [56, 57, 60]. The configuration of the *like*-isomer (*R*,1′*R*-**17**) was proved undoubtedly by the X-ray structure [56]. Furthermore, the samples of pure diastereomers **17** and **19** were later used for comparison in the stereochemical assignments of the chiral azaaromatic analogs **20** and **21**.

In all cases, the catalyzed reactions were completed within 7 days at 80°C, affording a good yield of the amino alcohols. The reaction mixtures were stirred under argon in a sealed test tube, and the applied reaction time was necessary to reach the maximum conversion (controlled by TLC). The uncatalyzed reaction of **15** with 1-phenylethylamine gave both regioisomers **17** and **18** in 4% yield only. Moreover, the $Sc(OTf)_3$-catalyzed ring opening in the absence of DIEA resulted in much poorer yield. Interestingly, when we run the reaction of **15** in the presence of $Zn(OAc)_2$ (weaker Lewis acid), β-amino alcohol **17** was formed regioselectively. The reaction of *rac-trans*-stilbene oxide (**16**) with (*S*)-1-phenylethylamine gave also separable diastereomers (*ca.* 1 : 1) of amino alcohol **19** [57, 58, 61] in 54% total yield (Scheme 2).

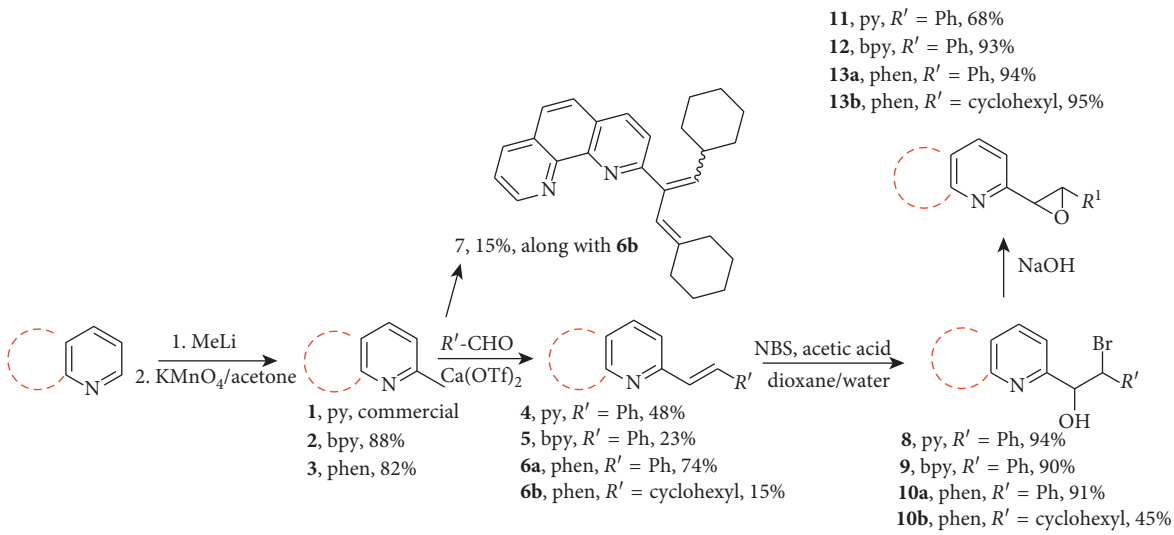
2.3. Selective Epoxide Ring Opening: Pyridine Derivatives. After the model studies, the epoxides with pyridine-type fragments were submitted to the ring-opening reactions. Unlike for styrene oxide (**15**), the reaction of *rac*-2-(oxiranyl)pyridine (**14**) with chiral amines gave only one regioisomer, β-amino alcohol **20**, regardless of the catalyst used. However, the better yield was observed for $Sc(OTf)_3$/DIEA (Scheme 3).

The product **20** consisted of two diastereomers (in *ca.* 1 : 1 ratio), which were smoothly separated by column chromatography. We ascribed their configuration comparing ^{1}H NMR spectra between the isolated diastereomers **20** and **17** (see supporting file S1), where similarities between their spectral patterns could be clearly seen.

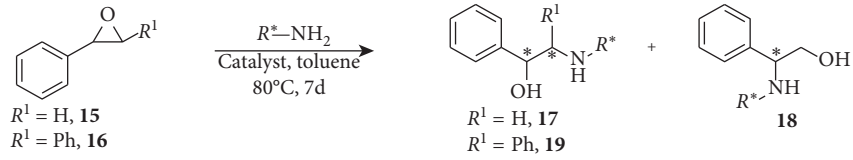
Other synthesized 2,3-disubstituted *trans* epoxides with the α-azaaromatic fragments (**11**–**13**) were submitted to the ring-opening reactions, and the results are summarized in Scheme 4 and Table 1.

The reaction of **11** and **12** with chiral 1-phenylethylamine carried out in the presence of $Sc(OTf)_3$/DIEA gave in each case only one regioisomer of the respective β-amino alcohol in good yield. The obtained products **21** and **23** consisted of two diastereomers (*ca.* 1 : 1), which were separated by column chromatography. Similarly, the reaction of **11** and **12** with (*R*)-1-cyclohexylethylamine gave regioselectively both amino alcohols **22** and **24**. For **22**, the diastereoisomers (obtained in nearly 1 : 1 ratio) were separated to give enantiomerically pure compounds (Table 1). For the obtained diastereomeric mixture of **24**, only (1*R*,2*R*,1′*R*)-**24** could be isolated as a stereochemically pure sample. The reaction of **13b** with (*R*)-1-phenylethylamine was sluggish, and the respective diastereomeric mixture **25** was formed in 8% yield. The reaction of *rac-trans*-2-(3-phenyloxiranyl)-1,10-phenanthroline (**13a**) with the same amine gave inseparable mixture, and the corresponding dehydration product could be detected only by ^{1}H NMR.

It is noteworthy that we observed different outcomes for the scandium-catalyzed ring opening of styrene oxide (**15**), where both regioisomers were formed (the model reaction, Scheme 2) and 2-oxiranyl-pyridines (Schemes 3 and 4), where only β-amino alcohols were obtained. The observed nucleophilic attack at the benzylic β-position (regioselectivity of aminolysis) can be explained by the specific interaction of scandium ion complexed to the pyridine nitrogen and oxiranyl oxygen atoms, thus supporting the formation of both diastereomers of one regioisomer **21** (Figure 1). This is corroborated by the results of DFT calculations for the simplified models of *trans*-**11** and its Sc^{3+} complex. The calculations indicated an increase of the length of Cβ-epoxide oxygen bond and a substantial rise of the Cβ positive charge as measured by ESP (electrostatic potential charge) (see supporting file S2). It should be noted that the

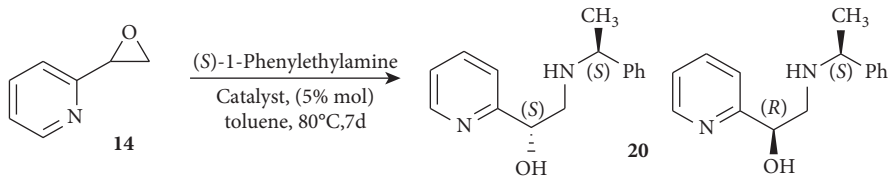


Scheme 1: Preparation of the α-azaarene epoxides.



R*-NH2	Epoxide	Catalyst	Product, isolated yield (%)		
(*S*)-1-Phenylethylamine	**15**	$Sc(OTf)_3$, DIEA	(*S*,1′*S*)-**17**, 19	(*R*,1′*S*)-**17**, 19	(*R*/*S*,1′*S*)-**18**, 38
(*S*)-1-Phenylethylamine	**16**	$Sc(OTf)_3$, DIEA	(1*S*,2*R*,1′*S*)-**19**, 27	(1*R*,2*S*,1′*S*)-**19**, 27	
(*R*)-1-Phenylethylamine	**15**	$Zn(OAc)_2$	(*R*,1′*R*)-**17**, 34	(*S*,1′*R*)-**17**, 34	
(*S*)-1-Phenylethylamine	**15**	$Zn(OAc)_2$	(*S*,1′*S*)-**17**, 34	(*R*,1′*S*)-**17**, 34	
(*S*)-1-Phenylethylamine	**15**	No catalyst	(*S*,1′*S*)-**17** and	(*R*,1′*S*)-**17** and	(*R*/*S*,1′*S*)-**18** (total 4%)

Scheme 2: Ring opening of styrene and stilbene oxides with chiral 1-phenylethylamine.



Catalyst	Product, isolated yield (%)	
$Zn(OAc)_2$	(*S*,1′*S*)-**20**, 17	(*R*,1′*S*)-**20**, 17 (total 34)
$Sc(OTf)_3$, DIEA	(*S*,1′*S*)-**20**, 36	(*R*,1′*S*)-**20**, 36 (total 72)
No catalyst	(*S*,1′*S*)-**20** and	(*R*,1′*S*)-**2** (1:1 by NMR, total 5)

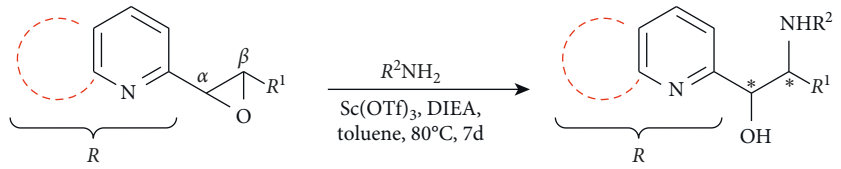
Scheme 3: Ring opening of 2-(oxiranyl)pyridine with (*S*)-1-phenylethylamine.

epoxide **11** has already been opened in the $MgBr_2$-supported reaction with the same regioselectivity. That result was explained by similar Mg^{2+} complexation [52].

In order to confirm the configurations of obtained new ring-opening products, we transformed the amino alcohols into their cyclic urethanes (Scheme 5).

The respective ^{1}H NMR spectral patterns are very similar for the known (4*R*,5*S*,1′*S*)-**26** [58] and new (4*R*,5*R*,1′S)-**27**. Their spectra substantially differ from that for (4*S*,5*S*,1′*S*)-**27** (Figure 2) (different configuration descriptors at C5 for (4*R*,5*R*,1′*S*)-**27** and (4*R*,5*S*,1′*S*)-**26** arise from CIP rules).

The obtained enantiomerically pure pyridine-β-amino alcohols: (*S*,1′*S*)-**20**, (1*S*,2*S*,1′*R*)-**21**, and (1*S*,2*S*,1′*S*)-**21** and bipyridine-β-amino alcohols: (1*S*,2*S*,1′*S*)-**23** and (1*R*,2*R*,1′*S*)-**23** were preliminarily assessed as chiral catalysts in the asymmetric aldol reaction [62] of *p*-nitrobenzaldehyde with cyclohexanone. The reaction conditions were optimized by screening chiral ligands and metal salts. The highest selectivity for the *anti*-aldol



11-13 **21-25**

Epoxide			Chiral amine	Product
R = pyrid-2-yl,	R^1 = Ph,	**11**	R^2 = 1-phenylethyl	**21**
R = pyrid-2-yl,	R^1 = Ph,	**11**	R^2 = 1-cyclohexylethyl	**22**
R = 2,2′-bipyrid-6-yl	R^1 = Ph,	**12**	R^2 = 1-phenylethyl	**23**
R = 2,2′-bipyrid-6-yl,	R^1 = Ph,	**12**	R^2 = 1-cyclohexylethyl	**24**
R = 1,10-phenanthrolin-2-yl,	R^1 = cyclohexyl,	**13b**	R^2 = 1-phenylethyl	**25**

Scheme 4: Ring opening of 2-oxiranyl-azaarenes with chiral amines.

Table 1: Ring opening of 2-oxiranyl-azaarenes with chiral amines.

Epoxide	Amine	Product, yield (%)[a]	Total yield (%)
11	(*S*)-1-Phenylethylamine	(1*S*,2*S*,1′*S*)-**21**, 26 (1*R*,2*R*,1′*S*)-**21**, 26	52
11	(*R*)-1-Phenylethylamine	(1*R*,2*R*,1′*R*)-**21**, 29 (1*S*,2*S*,1′*R*)-**21**, 29	58
11	(*R*)-1-Cyclohexylethylamine	(1*R*,2*R*,1′*R*)-**22**, 33 (1*S*,2*S*,1′*R*)-**22**, 33	66
12	(*S*)-1-Phenylethylamine	(1*S*,2*S*,1′*S*)-**23**, 30 (1*R*,2*R*,1′*S*)-**23**, 30	60
12	(*R*)-1-Cyclohexylethylamine	(1*R*,2*R*,1′*R*)-**24**, 32 (1*S*,2*S*,1′*R*)-**24**[b]	64
13b	(*R*)-1-Phenylethylamine	(1*R*,2*R*,1′*R*)-**25**, (1*S*,2*S*,1′*R*)-**25**[c]	8

[a]The yield of each isolated diastereomer. [b]Pure (1*S*,2*S*,1′*R*)-**24** could not be isolated (remained in a mixture). [c]The isolated 1 : 1 diastereomeric mixture was identified by HR-MS and ^{1}H NMR.

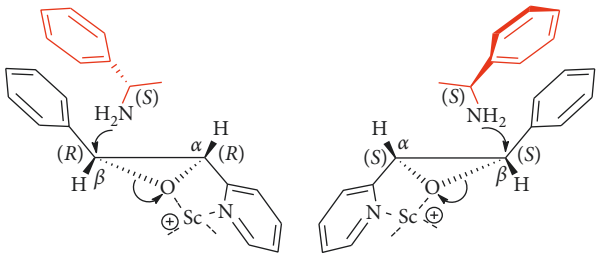
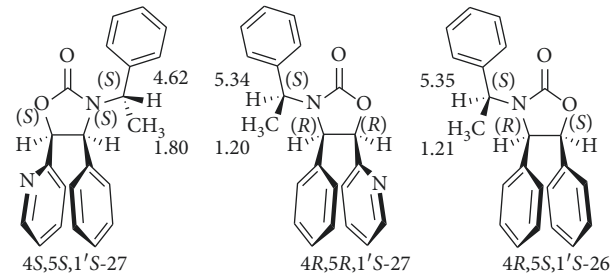
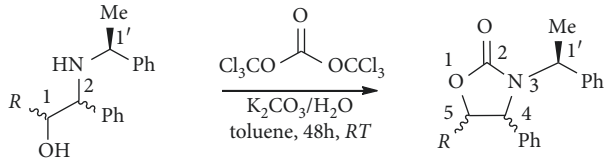


Figure 1: Models for regioselective aminolysis of *rac-trans*-**11**.



4*S*,5*S*,1′*S*-27 4*R*,5*R*,1′*S*-27 4*R*,5*S*,1′*S*-26

Figure 2: Structures and selected ^{1}H NMR (400 MHz, $CDCl_3$) resonances of oxazolidinones **26** and **27**.



(1*S*,2*R*,1′*S*)-19	R = Ph	(4*R*,5*S*,1′*S*)-26	59%
(1*S*,2*S*,1′*S*)-21	R = pyridin-2-yl	(4*S*,5*S*,1′*S*)-27	46%
(1*R*,2*R*,1′*S*)-21	R = pyridin-2-yl	(4*R*,5*R*,1′*S*)-27	46%

Scheme 5: Synthesis of oxazolidinones from β-amino alcohols.

(2*S*,1′*R*) 55% ee and 38% conversion was obtained with (1*R*,2*R*,1′*S*)-**23** and $Zn(OAc)_2$ + HOAc. For the details, see supporting file S3.

3. Conclusions

Concluding, we have developed an efficient synthesis of 2-oxiranyl-azaarenes designed as precursors of chiral ligands and synthetic building blocks. The regioselective epoxide ring opening with chiral primary amines in the presence of $Sc(OTf)_3$ and DIEA gave the corresponding β-amino alcohols, derivatives of pyridine and 2,2′-bipyridine. The resulting diastereomeric compounds were separated, and their stereochemical configurations were proved by correlation with the known analogs. The enantiomerically pure pyridine-β-amino alcohol was preliminarily tested as chiral ligands in the asymmetric aldol reaction with up to 55% ee outcome.

4. Experimental

4.1. General Information. Solvents were distilled, and other reagents were used as received. Reactions were monitored by thin-layer chromatography (TLC) on silica gel 60 F-254 or aluminum oxide F-25 (Type E) precoated plates, and spots were visualized with a UV lamp and/or Dragendorff reagent. Separation of products by chromatography was carried out on silica gel 60 (230–400 mesh) or aluminum oxide (neutral). Melting points were determined using an Electrothermal IA 91100 digital melting-point apparatus using the standard open capillary method and are uncorrected. Observed rotations at 589 nm were measured using an Optical Activity Ltd. Model AA-5 automatic polarimeter. ^{1}H and ^{13}C NMR spectra (400, 600 MHz and 100, 151 MHz, respectively) were collected on Jeol 400yh and Bruker Avance II 600 instruments. The spectra were recorded in $CDCl_3$ referenced to the respective residual signals of the solvent. Chemical shifts are given in parts per million (ppm) downfield from tetramethylsilane as the internal standard in a deuterated solvent and coupling constants (J) are in Hertz (Hz). Infrared spectra (4000–400 cm^{-1}) were collected on a Fourier transform, Bruker VERTEX 70V spectrometer using diamond ATR accessory. High-resolution mass spectra were recorded using electrospray ionization on Waters LCT Premier XE TOF instrument.

4.2. Synthesis of Methyl Derivatives

4.2.1. 6-Methyl-2,2′-bipyridine **2**. The methylation was performed according to the literature procedure [47]. Brown oil, 7.6 g, 88% yield, $R_f = 0.56$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.59–8.58 (m, 1H), 8.35–8.33 (m, 1H), 8.12 (d, $J = 7.8$ Hz, 1H), 7.69–7.66 (m, 1H), 7.59–7.56 (m, 1H), 7.17–7.15 (m, 1H), 7.04 (d, $J = 7.8$ Hz, 1H), 2.54 (s, 3H). The NMR data are in agreement with the reported ones [47].

4.2.2. 2-Methyl-1,10-phenanthroline **3**. The methylation was performed according to a modified literature procedure [48]. A solution of methyllithium in diethyl ether (1.6 M, 45 mL, 72 mmol) was added dropwise to a solution of 1,10-phenanthroline (10 g, 55 mmol) in toluene (200 mL) at −72°C under Ar atmosphere. The reaction mixture was stirred for 3 h at −72°C and for 2 h at room temperature. Then, ice was added with stirring in an ice-water bath and the resulting solution turned red. The aqueous layer was separated and extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed twice with brine and dried over Na_2SO_4, and ether was removed. The resulting orange toluene solution was treated with MnO_2 (54 g), stirred for 24 h, and then filtered through Celite. The solvent was removed *in vacuo* to give a crude product. Column chromatography on neutral alumina with *t*-butyl methyl ether (MTBE) as an eluent gave pure **3** (8.73 g 82%), as yellow crystals, m.p. 76–77°C (lit. [48] m.p. 75–76°C). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 9.17 (dd, $J = 4.2$, 1.8 Hz, 1H), 8.18 (dd, $J = 8.0$, 1.8 Hz, 1H), 8.08 (d, $J = 8.2$ Hz, 1H), 7.69 (q, $J = 8.8$ Hz, 2H), 7.56 (dd, $J = 8.2$, 4.6 Hz, 1H), 7.47 (d, $J = 8.2$ Hz, 1H), 2.92 (s, 3H). The NMR data are in agreement with the reported ones [48].

4.3. General Procedure for the Synthesis of 2-Styryl-azaarenes. The synthesis of 2-styryl-azaarenes was performed according to a modified literature procedure [50]. The mixture of 2-methylazaarene (1 mmol), benzaldehyde (1 mmol), and $Ca(OTf)_2$ [49] (5 mol%) was heated at 120°C under argon atmosphere for 48 h for α-picoline or 96 h for derivatives of bipyridine and phenanthroline. After the reaction completion (monitored by TLC), the mixture was dissolved in 1 M HCl and extracted with diethyl ether (3 × 15 mL). The remaining aqueous layer was alkalized with NaOH, extracted with diethyl ether (3 × 25 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give crude product.

4.3.1. 2-[(E)-2-Phenylethenyl]pyridine (**4**). White crystals, 88 mg, 48% yield, recrystallized (CH_2Cl_2/hexane), m.p. 89–90°C (lit. [51] m.p. 89–91°C), $R_f = 0.67$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.62–8.61 (m, 1H), 7.68–7.63 (m, 1H), 7.59–7.58 (m, 2H), 7.41–7.37 (m, 3H), 7.32–7.29 (m, 1H), 7.20 (s, 1H), 7.17–7.15 (m, 2H). The NMR data are in agreement with the reported ones [51].

4.3.2. 6-[(E)-2-Phenylethenyl]-2,2′-bipyridine (**5**). White crystals, 60 mg, 23% yield, recrystallized (CH_2Cl_2/hexane), m.p. 117–118°C, $R_f = 0.70$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.71 (d, $J = 6.0$ Hz, 1H), 8.59 (d, $J = 6.0$ Hz, 1H), 8.30 (d, $J = 7.8$ Hz, 1H), 7.89–7.86 (m, 1H), 7.82–7.77 (m, 2H), 7.64 (d, $J = 7.2$ Hz, 2H), 7.42–7.39 (m, 3H), 7.35–7.30 (m, 2H) 7.28–7.25 (m, 1H); ^{13}C NMR (600 MHz, $CDCl_3$) δ: 156.2, 155.6, 155.0, 148.9, 137.5, 137.1, 136.8, 132.9, 128.7, 128.3, 128.2, 127.2, 123.8, 122.2, 121.4, 119.6; HR-MS (ESI) $[C_{18}H_{14}N_2 + H]^+$ requires 259.1230; found 259.1223.

4.3.3. 2-[(E)-2-Phenylethenyl]-1,10-phenanthroline (**6a**). Brown oil, 210 mg, 74% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25), $R_f = 0.62$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 9.28 (dd, $J = 4.3$, 1.8 Hz, 1H), 8.29 (dd, $J = 8.2$, 1.8 Hz, 1H), 8.21 (d, $J = 8.2$ Hz, 1H), 7.95 (d, $J = 6.0$ Hz, 1H), 7.86–7.78 (m, 3H), 7.76–7.72 (m, 1H), 7.75 (d, $J = 6.0$ Hz, 2H), 7.67–7.65 (m, 1H), 7.42–7.40 (m, 2H) 7.34–7.31 (m, 1H); ^{13}C NMR (600 MHz, $CDCl_3$) δ: 156.6, 149.9, 145.5, 145.4, 136.8, 136.6, 136.4, 134.8, 129.5, 129.1, 128.8, 128.6, 127.6, 127.4, 126.7, 125.8, 122.9, 120.7; HR-MS (ESI) $[C_{20}H_{14}N_2 + H]^+$ requires 283.1230; found 283.1242.

4.3.4. 2-[(E)-2-Cyclohexylethenyl)-1,10-phenanthroline (**6b**). Yellow oil, 43 mg, 15% yield, purified by column chromatography (Al_2O_3, 20% AcOEt/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.20 (dd, $J = 4.6$, 1.8 Hz, 1H), 8.22 (dd, $J = 8.2$, 1.8 Hz, 1H), 8.13 (d, $J = 8.2$ Hz, 1H), 7.80 (d, $J = 8.2$ Hz, 1H), 7.72 (q, $J = 8.9$ Hz, 2H), 7.60 (dd, $J = 8.2$, 4.6 Hz, 1H), 7.01

(dd, $J = 16.2$, 1.2 Hz, 1H), 6.81 (dd, $J = 16.2$, 6.4 Hz, 1H), 2.30–2.24 (m, 1H), 1.92–1.88 (m, 2H), 1.82–1.77 (m, 2H), 1.72–1.66 (m, 1H), 1.41–1.16 (m, 5H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 157.4, 150.3, 146.2, 143.3, 136.3, 136.2, 129.6, 128.9, 127.3, 126.6, 126.5, 125.7, 122.8, 119.9, 41.2, 32.6, 26.3, 26.2; HR-MS (ESI) $[C_{20}H_{20}N_2 + H]^+$ requires 289.1699; found 289.1705.

4.3.5. 1-Cyclohexyl-3-cyclohexylidene-2-(1,10-phenonthrolin-2-yl)propene (**7**). Yellow oil, 42 mg, 15% yield, purified by column chromatography (Al_2O_3, 20% AcOEt/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.17 (dd, $J = 4.3$, 1.5 Hz, 1H), 8.20 (dd, $J = 7.9$, 1.8 Hz, 1H), 8.09 (d, $J = 8.2$ Hz, 1H), 7.73–7.66 (m, 3H), 7.59 (dd, $J = 7.9$, 4.3 Hz, 1H), 7.02 (dd, $J = 9.8$, 1.5 Hz, 1H), 6.05 (s, 1H), 2.46–2.43 (m, 1H), 2.34–2.31 (m, 2H), 1.96–1.93 (m, 2H), 1.77–1.75 (m, 4H), 1.69–1.63 (m, 3H), 1.55–1.50 (m, 2H), 1.40–1.31 (m, 7H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.4, 150.1, 146.4, 145.8, 144.9, 141.4, 136.11, 136.09, 134.6, 129.0, 127.3, 126.6, 125.4, 122.7, 121.9, 118.3, 39.1, 36.9, 32.4, 30.6, 28.8, 27.3, 26.7, 26.3, 26.2; HR-MS (ESI) $[C_{27}H_{30}N_2 + H]^+$ requires 383.2482; found 383.2483.

4.4. General Procedure for the Synthesis of Bromohydrins. The synthesis of bromohydrins was performed according to a modified literature procedure [53]. The mixture of 2-styryl-azaarene (3.0 mmol), NBS (587 mg, 3.3 mmol), and acetic acid (0.5 mL) was dissolved in the mixture of dioxane/water (3.5 mL/7 mL) and stirred at room temperature for 24 h. After completion of the reaction, the mixture was extracted with chloroform (3×30 mL). The combined organic layers were dried by over Na_2SO_4 filtered and concentrated *in vacuo* to give the desired product as confirmed by ^{1}H NMR.

4.4.1. 2-Bromo-1-phenyl-2-(pyridin-2-yl)ethanol (**8**). Brown oil, 784 mg, 94% yield; $R_f = 0.57$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.57–8.56 (m, 1H), 7.63–7.60 (m, 2H), 7.30–7.27 (m, 2H), 7.27–7.25 (m, 2H), 7.23–7.21 (m, 2H), 5.41 (d, $J = 5.4$ Hz, 1H), 5.20 (d, $J = 5.4$ Hz, 1H).

4.4.2. 2-Bromo-1-phenyl-2-(2,2′-bipyridin-6-yl)ethanol (**9**). White crystals, 960 mg, 90% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25), m.p. 117–118°C, $R_f = 0.61$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.72 (d, $J = 4.8$ Hz, 1H), 8.38–8.34 (m, 1H), 7.90 (s, 1H), 7.77–7.74 (t, $J = 7.8$ Hz, 1H), 7.40–7.38 (m, 1H), 7.32 (d, $J = 7.2$ Hz, 1H) 7.28–7.24 (m, 4H), 7.24–7.22 (m, 2H), 5.53 (d, $J = 5.4$ Hz, 1H), 5.28 (d, $J = 5.4$ Hz, 1H).

4.4.3. 2-Bromo-1-phenyl-2-(1,10-phenanthrolin-2-yl)ethanol (**10a**). Brown oil, 1.0 g, 91% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25), $R_f = 0.24$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 9.31–9.30 (m, 1H), 8.40 (d, $J = 7.8$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H), 7.87–7.83 (m, 2H), 7.78–7.75 (m, 2H), 7.55 (d, $J = 7.2$ Hz, 2H), 7.29–7.27 (m, 2H), 7.24–7.21 (m, 1H), 5.79 (d, $J = 6.6$ Hz, 1H), 5.60 (d, $J = 6.6$ Hz, 1H).

4.4.4. 2-Bromo-1-cyclohexyl-2-(1,10-phenanthrolin-2-yl)ethanol (**10b**). Yellow oil, 520 mg, 45% yield, purified by column chromatography (Al_2O_3, $CHCl_3$: AcOEt : hexane 1 : 1 : 2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.15 (dd, $J = 4.3$, 1.8 Hz, 1H), 8.25 (dd, $J = 8.2$, 1.8 Hz, 1H), 8.20 (d, $J = 8.2$ Hz, 1H), 7.81–7.75 (m, 3H), 7.63 (dd, $J = 8.2$, 4.6 Hz, 1H), 5.17 (d, $J = 9.2$ Hz, 1H), 4.36 (dd, $J = 9.5$, 2.4 Hz, 1H), 2.57 (s, 2H), 2.27–2.25 (m, 1H), 2.04–2.02 (m, 1H), 1.82–1.16 (m, 7H).

4.5. General Procedure for the Synthesis of Epoxides. The synthesis of epoxides was performed according to a modified literature procedure [53]. Bromohydrin (2.8 mmol) was dissolved in dioxane (3.5 mL), then 1 M aqueous NaOH (4.5 mL) was added, and the mixture was stirred at room temperature for 24 h. After completion of the reaction, the mixture was extracted with chloroform (3×30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give the desired product.

4.5.1. trans-2-(3-Phenyl-2-oxiranyl)pyridine (**11**). Brown oil, 375 mg, 68% yield, $R_f = 0.63$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.60–8.58 (m, 1H), 7.73–7.69 (m, 1H), 7.38–7.31 (m, 6H), 7.26–7.23 (m, 1H), 4.05 (AB system, 2H). The NMR data are in agreement with the reported ones [52].

4.5.2. trans-6-(3-Phenyl-2-oxiranyl)-2,2′-bipyridine (**12**). White crystals, 713 mg, 93% yield, m.p. 117–118°C, $R_f = 0.61$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). IR υ_{max} (Neat) 2960, 2926, 1580, 1563, 775, 760, 746, 694 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.7 (d, $J = 4.2$ Hz, 1H), 8.47 (d, $J = 7.8$ Hz, 1H), 8.4 (d, $J = 7.8$ Hz, 1H), 7.88–7.84 (m, 2H), 7.40–7.36 (m, 4H), 7.35–7.26 (m, 3H), 4.16 (d, $J = 1.8$ Hz, 1H), 4.12 (d, $J = 1.8$ Hz, 1H); ^{13}C NMR (600 MHz, $CDCl_3$) δ: 156.1, 155.8, 155.7, 149.1, 137.8, 137.0, 136.8, 128.6, 128.5, 125.8, 123.9, 121.4, 120.6, 119.7, 63.2, 61.9; HR-MS (ESI) $[C_{18}H_{14}N_2O + H]^+$requires 275.1179; found 275.1180.

4.5.3. trans-2-(3-Phenyl-2-oxiranyl)-1,10-phenanthroline (**13a**). Brown oil, 784 mg, 94% yield, $R_f = 0.44$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.25). IR υ_{max} (Neat) 2923, 2853, 1588, 1555, 845, 741, 696 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 9.18 (dd, $J = 4.3$, 1.8 Hz, 1H), 8.31–8.24 (m, 2H), 7.80 (d, $J = 1.8$ Hz, 2H), 7.63 (dd, $J = 8.2$, 6.4 Hz, 2H), 7.37–7.33 (m, 5H), 4.69 (d, $J = 1.8$ Hz, 1H), 4.02 (d, $J = 1.8$ Hz 1H); ^{13}C NMR (600 MHz, $CDCl_3$) δ: 158.0, 150.6, 146.0, 145.8, 137.5, 136.6, 136.3, 129.2, 128.7, 128.6, 128.1, 126.7, 126.6, 125.9, 123.3, 118.1, 64.0, 63.1; HR-MS (ESI) $[C_{20}H_{14}N_2O + H]^+$ requires 299.1135; found 299.1146.

4.5.4. trans-2-(3-Cyclohexyl-2-oxiranyl)-1,10-phenanthroline (**13b**). Yellow oil, 811 mg, 95% yield. ^{1}H NMR (400 MHz,

$CDCl_3$) δ: 9.24 (dd, $J = 4.3$, 1.5 Hz, 1H), 8.26 (dd, $J = 8.2$, 1.8 Hz, 1H), 8.22 (d, $J = 8.2$ Hz, 1H), 7.78 (s, 2H), 7.65 (dd, $J = 8.2$, 4.6 Hz, 1H), 7.45 (d, $J = 8.2$ Hz, 1H), 4.47 (d, $J = 2.1$ Hz, 1H), 2.96 (d, $J = 2.1$ Hz, 1H), 1.59–1.26 (m, 3H), 1.25–1.24 (m, 6H), 0.86–0.84 (m, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) δ: 159.2, 150.6, 137.1, 136.2, 134.3, 129.6, 129.1, 128.6, 126.6, 126.5, 123.1, 118.3, 38.9, 30.6, 24.1 23.0, 14.1, 11.2; HR-MS (ESI) $[C_{20}H_{20}N_2O + H]^+$ requires 305.1648; found 305.1653.

4.6. Procedures for Ring Opening of Epoxides

4.6.1. Method A (Catalyzed by $Sc(OTf)_3$). A solution of the epoxide **11, 12, 13b, 14, 15,** or **16** (0.5 mmol), 1-phenylethylamine (77 μL, 0.6 mmol), $Sc(OTf)_3$ (12 mg, 5 mol%), and *N*-ethyldiisopropylamine (170 μL, 1 mmol) in toluene (2 mL) was stirred under argon in a sealed test tube at 80°C for 7 days. The cooled mixture was directly submitted to the column chromatography on silica gel. In this way, the regioisomers **17** and **18**, resulting in the reaction of **15,** were separated, and their structures were confirmed by NMR. The isolated diastereoisomers **17**, as well as the respective diastereomers formed in the reactions of **11**, **12**, **14**, and **16**, were separated by column chromatography. Additionally, the diastereomers **17** could be separated by recrystallization from hexane/CH_2Cl_2.

The reactions of **11** (98 mg, 0.5 mmol) or **12** (137 mg, 0.5 mmol) with (*R*)-1-cyclohexylethylamine (88 μL, 0.6 mmol), $Sc(OTf)_3$ (12 mg, 5 mol%), and *N*-ethyldiisopropylamine (170 μL, 1 mmol) dissolved in toluene (2 mL) were run and then worked up as above. For the epoxide **11**, both diastereomers were separated by chromatography and gave pure samples, while for **12**, only one diastereomer (1*R*,2*R*,1′*R*)-**24** could be isolated in a pure form.

The pure separated products (*S*,1′*S*)-**17**, (*R*,1′*S*)-**17**, (*S*/*R*,1′S)-**18**, (1*R*,2*S*,1′*S*)-**19**, (1*S*,2*R*,1′*S*)-**19**, (*S*,1′*S*)-**20**, (*R*,1′*S*)-**20**, (1*R*,2*S*,1′*S*)-**21**, (1*S*,2*S*,1′*S*)-**21**, (1*S*,2*R*,1′*R*)-**19**, (1*R*,2*R*,1′*R*)-**21**, (1*S*,2*R*,1′*R*)-**22**, (1*R*,2*R*,1′*R*)-**22**, (1*R*,2*S*,1′*S*)-**23**, (1*S*,2*S*,1′*S*)-**23**, (1*R*,2*R*,1′*R*)-**24**, and [(1*R*,2*R*,1′*R*)- and (1*S*,2*S*,1′*R*)]-**25** were analyzed, and their properties are reported below.

4.6.2. Method B (Catalyzed by $Zn(OAc)_2$). The reaction was carried out under the same conditions as in Method A, but instead of $Sc(OTf)_3$ and *N*-ethyldiisopropylamine, $Zn(OAc)_2$ (4.6 mg, 5 mol%) as a catalyst was added. The products (*R*,1′*R*)-**17**, (*S*,1′*R*)-**17**, (*S*,1′*S*)-**17**, (*R*,1′*S*)-**17**, (*S*,1′*S*)-**20**, and (*R*,1′*S*)-**20** were isolated as in Method A.

4.6.3. Method C (Absence of a catalyst). The reaction of **14** or **15** (1.0 mmol) with 1-phenylethylamine (154 μL, 1.2 mmol) dissolved in toluene (4 mL) was carried out under argon in a sealed test tube at 80°C for 7 days. After the same workup as in Method A (direct chromatography), the products were analyzed by NMR.

*(1) (R,R)-2-(1-Phenylethyl)amino-1-phenyl-ethanol (R,1′R)-***17**. White crystals, 41 mg, 34% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1), m.p. 145–146°C (lit. [60] m.p. 145–148°C), $[\alpha]_D^{20} = 26$ (*c* 1.0, $CHCl_3$), (lit. [60] $[\alpha]_D^{20} = 26.5$ (*c* 1.0, $CHCl_3$)), $R_f = 0.20$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34–7.22 (m, 10H), 4.72 (dd, $J = 8.9$, 3.7 Hz, 1H), 3.75 (q, $J = 6.4$ Hz, 1H), 2.64 (dd, $J = 12.2$, 3.7 Hz, 1H), 2.54 (dd, $J = 12.2$, 8.9 Hz, 1H), 1.38 (d, $J = 6.7$ Hz, 3H). The NMR data are in agreement with literature data for (*R*,1′*R*)-enantiomer [60].

*(2) (S,R)-2-(1-Phenylethyl)amino-1-phenyl-ethanol (S,1′R)-***17**. Brown crystals, 41 mg, 34% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1), $R_f = 0.25$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34–7.22 (m, 10H), 4.55 (dd, $J = 8.9$, 3.7 Hz, 1H), 3.81 (q, $J = 6.4$ Hz, 1H), 2.81 (dd, $J = 12.2$, 3.7 Hz, 1H), 2.54 (dd, $J = 12.2$, 8.9 Hz, 1H), 1.36 (d, $J = 6.7$ Hz, 3H). The NMR data are in agreement with literature data for (*R*,1′*S*)-enantiomer [60].

*(3) (S,S)-2-(1-Phenylethyl)amino-1-phenyl-ethanol (S,1′S)-***17**. White crystals, 41 mg, 34% yield, recrystallized (CH_2Cl_2/hexane), $R_f = 0.20$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34–7.22 (m, 10H), 4.60 (dd, $J = 8.9$, 3.7 Hz, 1H), 3.77 (q, $J = 6.4$ Hz, 1H), 2.77 (dd, $J = 12.2$, 3.7 Hz, 1H), 2.63 (dd, $J = 12.2$, 8.9 Hz, 1H), 1.40 (d, $J = 6.7$ Hz, 3H). The NMR data are in agreement with literature data for (*R*,1′*R*)-enantiomer [60].

*(4) (R,S)-2-(1-Phenylethyl)amino-1-phenyl-ethanol (R,1′S)-***17**. Brown crystals, 41 mg, 34% yield, recrystallized (CH_2Cl_2/hexane), m.p. 82–83°C (lit. [60] m.p. 80–85°C), $[\alpha]_D^{20} = -105$ (*c* 1.0, $CHCl_3$), (lit. [60] $[\alpha]_D^{20} = -110$ (*c* 1.0, $CHCl_3$)), $R_f = 0.25$ ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34–7.21 (m, 10H), 4.74 (dd, $J = 9.2$, 3.4 Hz, 1H), 3.83 (q, $J = 6.7$ Hz, 1H), 2.79 (dd, $J = 12.2$, 3.7 Hz, 1H), 2.55 (dd, $J = 12.2$, 9.2 Hz, 1H), 1.40 (d, $J = 6.4$ Hz, 3H). The NMR data are in agreement with literature data for (*R*,1′*S*)-enantiomer [60].

*(5) (R/S,1′S)-2-(1′-Phenylethyl)amino-2-phenyl-ethanol (S,1′S)-***18** *and (R,1′S)-* **18***, (1 : 1).* Colorless oil, 46 mg, 38% total yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40–7,18 (m, 20H), 3.90–3.88 (m, 1H), 3.77–3.71 (m, 2H), 3.65–3.67 (m, $J = 6.7$ Hz, 1H), 3.58–3.50 (m, 4H), 1.36 (d, $J = 6.4$ Hz, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.31, 128.30, 127.90, 127.85, 127.8, 127.7, 127.5, 127.3, 127.2, 126.8, 66.1, 65.9, 62.5, 61.7, 55.5, 55.1, 24.1, 22.2; HR-MS (ESI) $[C_{16}H_{19}NO + H]^+$ requires 242.1539; found 242.1545. The NMR data are in agreement with the reported ones [59].

(6) (1R,2R,1′S)-2-(1′-Phenylethyl)amino-1,2-diphenyl-ethanol (1R,2S,1′S)- **19**. White crystals, 43 mg, 27% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1), m.p. 135–136°C, $[\alpha]_D^{20} = -63$ (*c* 0.9, $CHCl_3$), (lit. [58] $[\alpha]_D^{20} = -66.1$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33–7.13 (m, 11H), 6.98–6.94 (m, 4H), 4.98 (d,

J = 4.9 Hz, 1H), 4.0 (d, J = 4.9 Hz, 1H), 3.78 (q, J = 6.4 Hz, 1H), 1.35 (d, J = 6.7 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 145.5, 140.5, 139.2, 128.6, 128.2, 128.1, 127.8, 127.5, 127.3, 127.2, 126.6, 126.5, 75.4, 65.6, 54.6, 23.1. The NMR data are in agreement with literature data for (1*R*,2*S*,1′*S*)-enantiomer [58].

(7) (1S,2R,1′S)-2-(1′-Phenylethyl)amino-1,2-diphenyl-ethanol (1S,2R,1′S)- **19**. Colorless oil, 43 mg, 27% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1), $[\alpha]_D^{20}$ = –111 (*c* 1.0, $CHCl_3$), (lit. [58] $[\alpha]_D^{20}$ = –112.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$); δ: 7.33–7.20 (m, 10H), 7.09–6.95 (m, 5H), 4.64 (d, J = 4.9 Hz, 1H), 3.62 (d, J = 4.9 Hz, 1H), 3.49 (q, J = 6.4 Hz, 1H), 1.23 (d, J = 6.7 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 144.9, 140.5, 139.7, 128.5, 128.4, 128.1, 127.8, 127.7, 127.2, 127.1, 126.7, 126.4, 75.6, 65.8, 54.9, 24.8. The NMR data are in agreement with literature data for (1*S*,2*R*,1′*S*-)-enantiomer [58].

(8) (S,S)-2-(1-Phenylethyl)amino-1-(pyridin-2-yl)ethanol (S,1′S)- **20**. White crystals, 44 mg, 36% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1), m.p. 119–120°C, $[\alpha]_D^{20}$ = –42 (*c* 0.6, CH_2Cl_2). IR υ_{max} (Neat) 3290, 2971, 1589, 1432, 703 cm^1; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50–8.48 (m, 1H), 7.64 (td, J = 7.4, 1.8 Hz, 1H), 7.33–7.22 (m, 6H), 7.17–7.14 (m, 1H), 4.71 (dd, J = 8.1, 3.7 Hz, 1H), 3.75 (q, J = 6.5 Hz, 1H), 2.86 (dd, J = 12.0, 3.7 Hz, 1H), 2.69 (dd, J = 12.0, 8.1 Hz, 1H), 1.36 (d, J = 6.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 161.0, 148.5, 145.5, 136.7, 128.6, 127.1, 126.7, 122.4, 120.6, 72.3, 58.6, 54.4, 24.4; HR-MS (ESI) $[C_{15}H_{18}N_2O + H]^+$ requires 243.1492; found 243.1500.

(9) (R,S)-2-(1-Phenylethyl)amino-1-(pyridin-2-yl)ethanol (R,1′S)- **20**. White crystals 44 mg, 36% yield, purified by column chromatography (SiO_2, $CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1), m.p. 75–76°C, $[\alpha]_D^{20}$ = –52 (*c* 0.8, CH_2Cl_2). IR υ_{max} (Neat) 3081, 2847, 1588, 1433, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.48–8.46 (m, 1H), 7.63 (td, J = 7.6, 1.8 Hz, 1H), 7.37–7.21 (m, 6H), 7.15 (m, 1H) 4.97 (dd, J = 8.1, 3.7 Hz, 1H), 3.96 (q, J = 6.5 Hz, 1H), 3.08 (dd, J = 12.0, 3.7 Hz, 1H), 2.68 (m, J = 12.0, 8.1 Hz, 1H), 1.50 (d, J = 6.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 160.4, 148.3, 136.9, 128.8, 127.8, 127.1, 127.0, 122.6, 120.8, 70.9, 58.5, 53.3, 23.3; HR-MS (ESI) $[C_{15}H_{18}N_2O + H]^+$ requires 243.1492; found 243.1504.

(10) (1S,2S,1′S)-2-(1′-Phenylethyl)amino-2-phenyl-1-(pyridin-2-yl)ethanol (1S,2S,1′S)- **21**. White crystals, 42 mg, 26% yield, purified by column chromatography (SiO_2, AcOEt : $CHCl_3$ 8 : 2), m.p. 94–95°C, $[\alpha]_D^{20}$ = –78 (*c*1.0, CH_2Cl_2), R_f = 0.35 ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). IR υ_{max} (Neat) 3147, 3032, 2924, 1592, 1433, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.36–8.34 (m, 1H), 7.47 (td, J = 7.6, 1.5 Hz, 1H), 7.29–7.24 (m, 4H), 7.24–7.19 (m, 1H), 7.14–7.09 (m, 3H), 7.06–6.94 (m, 4H), 5.12 (d, J = 4.3 Hz, 1H), 4.15 (d, J = 4.3 Hz, 1H), 3.81 (q, J = 6.4 Hz, 1H) 1.35 (d, J = 6.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.6, 148.0, 145.77, 138.9, 136.5, 128.6, 128.2, 127.9, 127.2, 127.1, 126.7, 122.2, 121.5, 74.9, 65.1, 54.8, 23.1; HR-MS (ESI) $[C_{21}H_{22}N_2O + H]^+$ requires 319.1805; found 319.1801.

(11) (1R,2R,1′S)-2-(1′-Phenylethyl)amino-2-phenyl-1-(pyridin-2-yl)ethanol(1R,2R,1′S)- **21**. Colorless oil, 42 mg, 26% yield, purified by column chromatography (SiO_2, AcOEt : $CHCl_3$ 8 : 2), $[\alpha]_D^{20}$ = –93 (*c* 1.0, CH_2Cl_2), R_f = 0.48 ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). IR υ_{max} (Neat) 3324, 3026, 2923, 1592, 1451, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, J = 4.6 Hz, 1H), 7.47 (td, J = 7.6, 1.5 Hz, 1H), 7.26–7.12 (m, 9H), 6.96–6.95 (m, 3H), 4.88 (s, 1H), 4.20 (s, 1H), 3.77 (d, J = 4.9 Hz, 1H), 3.57 (q, J = 6.7 Hz, 1H), 1.30 (d, J = 6.7 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.5, 148.0, 145.4, 139.2, 136.0, 128.4, 128.3, 128.0, 127.2, 126.90, 126.89, 122.4, 121.8, 76.2, 65.4, 54.9, 25.2; HR-MS (ESI) $[C_{21}H_{22}N_2O + H]^+$ requires 319.1805; found 319.1796.

(12) (1R,2R,1′R)-2-(1′-Phenylethyl)amino-2-phenyl-1-(pyridin-2-yl)ethanol (1R,2R,1′R)- **21**. White crystals, 46 mg, 29% yield, purified by column chromatography (SiO_2, AcOEt : $CHCl_3$ 8 : 2), m.p. 94–95°C, $[\alpha]_D^{20}$ = 78 (*c* 0.9, CH_2Cl_2), R_f = 0.35 ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). IR υ_{max} (Neat) 3133, 3032, 2922, 1592, 1434, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.37–8.35 (m, 1H), 7.47 (td, J = 7.6, 1.5 Hz, 1H), 7.32–7.20 (m, 5H), 7.25–7.10 (m, 3H), 7.06–7.03 (m, 1H), 6.99–6.93 (m, 3H), 5.10 (d, J = 4.3 Hz, 1H), 4.11 (d, J = 4.3 Hz, 1H), 3.80 (q, J = 6.4 Hz, 1H) 1.34 (d, J = 6.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.6, 148.1, 145.8, 139.9, 136.0, 128.6, 128.1, 127.9, 127.2, 127.1, 126.7, 122.2, 121.5, 74.9, 65.1, 54.7, 23.1; HR-MS (ESI) $[C_{21}H_{22}N_2O + H]^+$ requires 319.1805; found 319.1826.

(13) (1S,2S,1′R)-2-(1′-Phenylethyl)amino-2-phenyl-1-(pyridin-2-yl)ethanol(1S,2S,1′R)- ***21***. Colorless oil, 46 mg, 29% yield, purified by column chromatography (SiO_2, AcOEt : $CHCl_3$ 8 : 2), $[\alpha]_D^{20}$ = 93 (*c* 0.8, CH_2Cl_2), R_f = 0.48 ($CHCl_3$: AcOEt : MeOH 1 : 1 : 0.1). IR υ_{max} (Neat) 3322, 3026, 2923, 1593, 1451, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, J = 4.9 Hz, 1H), 7.49 (td, J = 7.2, 1.2 Hz, 1H), 7.28–7.06 (m, 9H), 6.98–6.90 (m, 3H), 4.88 (d, J = 4.9 Hz, 1H), 4.22 (s, 1H), 3.76 (d, J = 4.9 Hz, 1H), 3.57 (q, J = 6.7 Hz, 1H) 1.30 (d, J = 6.7 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.5, 148.0, 145.3, 139.2, 136.0, 128.4, 128.3, 128.0, 127.2, 126.90, 126.89, 122.4, 121.8, 76.2, 65.4, 54.9, 25.2; HR-MS (ESI) $[C_{21}H_{22}N_2O + H]^+$ requires 319.1805; found 319.1811.

(14) (1R,2R,1′S)-2-(1′-Cyclohexylethyl)amino-2-phenyl-1-(pyridin-2-yl)ethanol (1R,2R,1′R)- **22**. Brown oil, 53 mg, 33% yield, purified by column chromatography (SiO_2 20% MTBE/hexane), $[\alpha]_D^{20}$ = –45 (*c* 0.7, CH_2Cl_2). IR υ_{max} (Neat) 3139, 3019, 2924, 1435, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.46–8.44 (m, 1H), 7.43 (dq, J = 7.6, 1.8 Hz, 1H), 7.14–7.01 (m, 6H), 6.93 (d, J = 7.9 Hz, 1H), 4.95 (d, J = 4.6 Hz, 1H), 4.18 (d, J = 4.6 Hz, 1H), 2.55–2.52 (m, 1H), 1.72–1.63 (m, 8H), 1.28–1.16 (m, 3H), 0.97 (d, J = 6.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 160.3, 148.2, 140.1, 136.0, 128.0, 127.8, 127.2, 122.1, 121.5, 75.02, 65.25, 55.0, 42.8, 29.8, 28.1, 26.9, 26.8, 26.7, 17.8; HR-MS (ESI) $[C_{21}H_{28}N_2O + H]^+$ requires 325.2274; found 325.2280.

(15) (1S,2S,1′R)-2-(1′-Cyclohexylethyl)amino-2-phenyl-1-(pyridin-2-yl)ethanol (1S,2S,1′R)- **22**. Brown oil, 53 mg, 33% yield, purified by column chromatography (SiO_2 20% MTBE/hexane), $[\alpha]_D^{20} = 28$ (*c* 0.8, CH_2Cl_2). IR υ_{max} (Neat) 3062, 3028, 2925, 1434, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.42–8.40 (m, 1H), 7.48 (dq, $J = 7.6$, 1.8 Hz, 1H), 7.15–6.97 (m, 7H), 4.97 (d, $J = 4.6$ Hz, 1H), 4.19 (d, $J = 4.6$ Hz, 1H), 2.34–2.31 (m, 1H), 1.73–1.70 (m, 7H), 1.40–0.97 (m, 4H), 0.92 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.8, 148.1, 138.9, 136.0, 128.4, 127.8, 127.1, 122.2, 121.6, 76.2, 65.0, 54.0, 43.9, 29.6, 28.7, 26.8, 26.7, 26.6, 16.7; HR-MS (ESI) $[C_{21}H_{28}N_2O + H]^+$ requires 325.2274; found 325.2289.

(16) (1R,2R,1′S)-2-(1′-Phenylethyl)amino-2-phenyl-1-(2,2′-bipyridin-6-yl)ethanol (1R,2R,1′S)- **23**. Colorless oil, 60 mg, 30% yield, purified by column chromatography (Al_2O_3, MTBE), $R_f = 0.48$ (Al_2O_3, MTBE), $[\alpha]_D^{20} = -112$ (*c* 0.9, CH_2Cl_2). IR υ_{max} (Neat) 3324, 3026, 2924, 1564, 1430, 699 cm^{-1} ^1H NMR (400 MHz, $CDCl_3$) δ: 8.64–8.62 (m, 1H), 8.21 (dd, $J = 7.9$, 0.9 Hz, 1H), 8.05 (td, $J = 7.9$, 1.2 Hz, 1H), 7.74 (dd, $J = 7.9$, 1.8 Hz, 1H), 7.65 (t, $J = 7.6$ Hz, 1H), 7.29–7.13 (m, 9H), 7.0–6.98 (m, 3H), 4.95 (s, 1H), 4.22 (br s, 1H), 3.80 (d, $J = 4.9$ Hz, 1H), 3.59 (q, $J = 6.4$ Hz, 1H), 1.30 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 158.8, 155.8, 154.5, 149.2, 145.3, 139.3, 137.2, 136.8, 128.4, 128.3, 128.0, 127.2, 126.9, 126.8, 123.8, 121.9, 121.1, 119.7, 76.2, 65.4, 54.8, 25.2; HR-MS (ESI) $[C_{26}H_{25}N_3O + H]^+$ requires 396.2070; found 396.2067.

(17) (1S,2S,1′S)-2-(1′-Phenylethyl)amino-2-phenyl-1-(2,2′-bipyridin-6-yl)ethanol (1S,2S,1′S)- **23**. Colorless oil, 60 mg, 30% yield, purified by column chromatography (Al_2O_3, MTBE), $R_f = 0.39$ (Al_2O_3 MTBE), $[\alpha]_D^{20} = 7.2$ (c 0.6, CH_2Cl_2). IR υ_{max} (Neat) 3326, 3025, 2923, 1581, 1564, 1453, 1430, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.62–8.60 (m, 1H), 8.18 (d, $J = 6.7$ Hz, 1H), 7.97 (d, $J = 7.9$ Hz, 1H), 7.67 (td, $J = 7.6$, 1.8 Hz, 1H), 7.63 (t, $J = 7.6$ Hz, 1H), 7.31–7.23 (m, 6H), 7.11–6.94 (m, 3H), 7.01 (d, $J = 7.6$ Hz, 1H), 6.96–6.94 (m, 2H), 5.14 (d, $J = 3.9$ Hz, 1H), 4.21 (d, $J = 4.3$ Hz, 1H), 3.82 (q, $J = 6.4$ Hz, 1H), 1.35 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 158.9, 155.8, 154.5, 149.1, 145.9, 138.9, 137.2, 136.8, 129.6, 128.1, 127.9, 127.2, 127.1, 126.8, 123.8, 121.7, 121.1, 119.6, 74.9, 65.2, 54.6, 22.8; HR-MS (ESI) $[C_{26}H_{25}N_3O + H]^+$ requires 396.2070; found 396.2073.

(18) (1R,2R,1′R)-2-(1′-Cyclohexylethyl)amino-2-phenyl-1-(2,2′-bipyridin-6-yl)ethanol (1R,2R,1′R)- **24**. Colorless oil, 64 mg, 32% yield, purified by column chromatography (Al_2O_3, 20% MTBE/hexane). $[\alpha]_D^{20} = -37$ (*c* 0.9, CH_2Cl_2). IR υ_{max} (Neat) 3062, 2925, 2852, 1562, 1428, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.66–8.64 (m, 1H), 8.25 (td, $J = 7.9$, 1.2 Hz, 1H), 8.19 (dd, $J = 7.6$, 0.9 Hz, 1H) 7.79 (td, $J = 7.3$, 1.8 Hz, 1H), 7.66–7.58 (m, 1H), 7.31–7.27 (m, 1H), 7.15–6.97 (m, 6H), 5.00 (d, $J = 4.6$ Hz, 1H), 4.22 (d, $J = 4.6$ Hz, 1H), 2.54–2.51 (m, 1H), 1.71–1.61 (m, 6H), 1.41–1.32 (m, 1H), 1.25–1.21 (m, 1H), 1.16–0.97 (m, 3H), 0,95 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.5, 156.1, 154.5, 149.2, 140.3, 137.1, 136.8, 128.1, 127.9, 127.1, 123.7, 121.7, 121.1, 119.5, 76.3, 65.6, 65.0, 55.1, 42.7, 29.9, 27.9, 26.8, 26.7, 17.8; HR-MS (ESI) $[C_{26}H_{31}N_3O + H]^+$ requires 402.2540; found 402.2538.

(19) 2-(1′-Phenylethyl)amino-2-cyclohexyl-1-(1,10-phenanthrolin-2-yl)ethanol (1R,2R,1′R)- **25** *and (1S,2S,1′R)-* **25**. Colorless oil, 17 mg, 8% total yield, purified by column chromatography (SiO_2, hexane : AcOEt : $CHCl_3$ 2 : 1 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ: 9.16–9.14 (m, 2H), 8.22 (dd, $J = 7.9$, 1.8 Hz, 2H), 8.17 (d, $J = 8.2$ Hz, 1H), 8.13 (d, $J = 8.2$ Hz, 1H), 7.75 (d, $J = 1.8$ Hz, 4H), 7.62–7.58 (m, 2H), 7.52 (d, $J = 8.2$ Hz, 1H), 7.35–7.14 (m, 11H), 3.96 (d, $J = 3.1$ Hz, 1H), 3.89 (dd, $J = 7.9$, 3.4 Hz, 1H), 3.24 (s, 1H), 3.22 (d, $J = 2.1$ Hz, 1H), 1.79–1.49 (m, 11H), 1.41–1.39 (m, 6H), 1.29–1.19 (m, 9H), 1.10–1.09 (m, 4H); HR-MS (ESI) $[C_{28}H_{31}N_3O + H]^+$ requires 426.2540; found 426.2532.

4.7. General Procedure for the Synthesis of Oxazolidinones from Amino Alcohols. The synthesis of oxazolidinones was performed according to the literature procedure [58]. Triphosgene (36 mg, 0.12 mmol) was added to a mixture of the amino alcohol (0.3 mmol) in toluene (3 mL) and potassium carbonate (57 mg, 0.41 mmol) in water (1.3 mL) with vigorous stirring at room temperature. After being stirred for 48 h, the mixture was washed with water and brine, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was chromatographed on silica gel (hexane/ethyl acetate 7 : 3) to give the corresponding oxazolidinone.

*4.7.1. (4R,5S,1′S)-N-(1′-Phenylethyl)-4,5-diphenyl-2-oxazolidinone (4R,5S,1′S)-***26**. White crystals, 60 mg, 59% yield, m.p. 154–157°C (lit. [58] m.p. 154–156°C), $[\alpha]_D^{20} = 19.0$ (*c* 1.0, $CHCl_3$) (lit. [58] $[\alpha]_D^{20} = 19.1$ *c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.39–7.32 (m, 6H), 7.07–7.02 (m, 6H), 6.95–6.94 (m, 3H), 5.66 (d, $J = 8.2$ Hz, 1H), 5.35 (q, $J = 7.3$ Hz, 1H), 4.56 (d, $J = 8.2$ Hz, 1H), 1.21 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 158.1, 140.1, 136.6, 134.4, 128.9, 128.3, 128.2, 128.11, 128.07, 127.9, 127.8, 127.5, 126.0, 80.3, 62.8, 53.4, 18.3. The NMR data are in agreement with the literature [58].

*4.7.2. (4R,5R,1′S)-N-(1′-Phenylethyl)-5-pyridin-2-yl-4-phenyl-2-oxazolidinone (4R,5R,1′S)-***27**. White crystals, 47 mg, 46% yield, m.p. 120–122°C, $[\alpha]_D^{20} = 21$ (*c* 0.8, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ: 8.24–8.22 (m, 1H), 7.49–7.29 (m, 7H), 7.13 (d, $J = 7.6$ Hz, 1H), 7.05–7.03 (m, 3H), 6.92–6.89 (m, 2H), 5.71 (d, $J = 7.9$ Hz, 1H), 5.34 (q, $J = 7.0$ Hz, 1H), 4.79 (d, $J = 8.2$ Hz, 1H), 1.20 (d, $J = 7.34$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 157.7, 154.9, 148.7, 139.9, 136.9, 136.3, 128.9, 128.22, 128.19, 128.1, 127.8, 127.4, 122.4, 120.9, 80.6, 61.9, 53.5, 18.2; HR-MS (ESI) $[C_{22}H_{20}N_2O_2 + H]^+$ requires 345.1598; found 345.1618.

*4.7.3. (4S,5S,1′S)-N-(1′-Phenylethyl)-5-pyridin-2-yl-4-phenyl-2-oxazolidinone (4S,5S,1′S)-***27**. White crystals, 47 mg, 46% yield, m.p. 136–137°C, $[\alpha]_D^{20} = 16$ (*c* 0.6, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ: 8.23–8.22 (m, 1H), 7.39 (t, $J = 7.9$ Hz, 1H), 7.20–7.12 (m, 6H), 6.93–6.88 (m, 4H), 6.74–6.71 (m, 2H), 5.81 (d, $J = 8.2$ Hz, 1H), 5.07 (d, $J = 8.6$ Hz, 1H), 4.62 (q, $J = 7.0$ Hz, 1H), 1.60 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 157.4, 155.3, 148.6, 140.4, 136.3, 134.9, 128.4, 127.93, 127.91, 127.82, 127.80, 127.5, 122.5, 120.9, 79.8, 64.0,

54.6, 18.9; HR-MS (ESI) $[C_{22}H_{20}N_2O_2 + H]^+$ requires 345.1598; found 345.1601.

Data Availability

All the related data are included in the main text and supplementary files.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Supplementary Materials

This file includes NMR and IR spectra of compounds, a comparison of the ^{1}H NMR and ^{13}C NMR for known and new compounds, DFT computations for ring opening of aryl-heteroaryl-epoxide, and aldol reactions—experimental details and compound characterization. (*Supplementary Materials*)

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