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Efficient Direct Synthesis of Aziridine-Containing Chiral Tridentate Ligands by the Iminium-Mediated Self-Ring Opening Reaction of Enantiopure Aziridines and Salicylaldehydes

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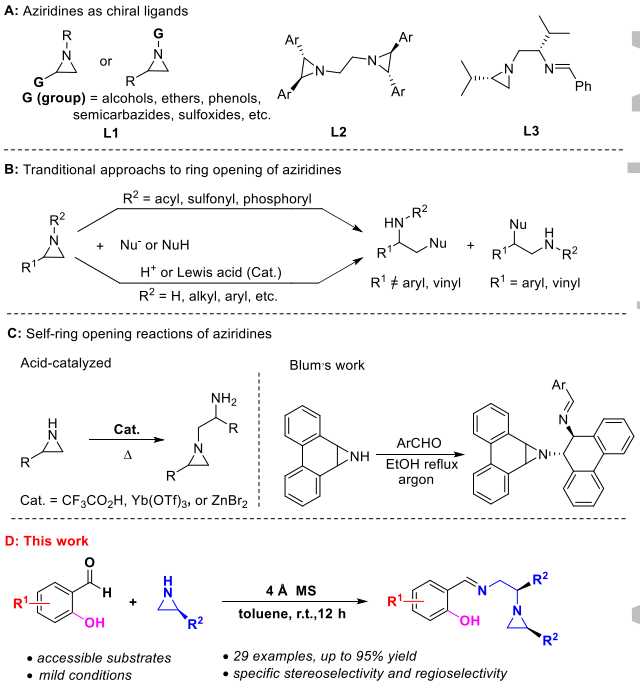
Abstract. An efficient method for the direct synthesis of aziridine-containing chiral tridentate ligands was developed from enantiopure aziridines and salicylaldehydes. The method achieved the regiospecific cleavage of more substituted C-N bonds of aziridines through an iminium-mediated self-ring opening reaction of aziridines with up to 95% yield and complete inversion of configuration. The (*S*)-2-alkylaziridine-derived tridentate ligands displayed excellent activity and stereoselectivity in the zinc trifluoromethanesulfonate-catalyzed asymmetric aldol reactions of acetone and aromatic aldehydes.

Keywords: iminium-mediated; self-ring opening; aziridine; chiral tridentate ligand; asymmetric aldol reaction.

Introduction

Aziridines and their derivatives play a crucial role in the development of three-membered heterocyclic chemistry.[1] Functionalized aziridines are abundantly present in biologically active natural products and synthetic drugs[2] and have been widely used as important intermediates in organic synthesis.[3] They have also been applied as chiral transfer reagents.[4] Moreover, with the rapid development of asymmetric synthesis and catalysis, aziridines have been utilized as chiral auxiliary agents and chiral ligands, respectively.[5] In recent years, the investigations on aziridine-derived chiral ligands have focused on chiral aziridine-containing alcohols,[6] ethers,[7] phenols,[8] semicarbazides,[9] and sulfoxides[10] (**L1**). Bis-aziridine ligands **L2** have also been synthesized and applied in various asymmetric reactions.[11] Recently, Pieczonka's group prepared chiral bidentate aziridine-derived imine ligands (**L3**) through the Lewis acid $ZnBr_2$-catalyzed self-ring opening of aziridines followed by condensation with benzaldehyde (Scheme 1 **A**).[12] However, only limited aziridine-derived chiral ligands and their application have been reported to date due to their complicated and multiple synthetic steps. Therefore, in order to enrich the use of aziridine-derived chiral ligands, it is in demand to develop new aziridine-containing chiral ligands and their efficient synthetic methods.



Scheme 1. Aziridines as Chiral Ligands and Their Ring Opening Reactions.

Similar to other three-membered heterocycles,[13] aziridines are very susceptible to open their rings due to their unique ring tension. Aziridines are mainly classified into two different groups on the basis of their activities in the ring opening reactions: 1)

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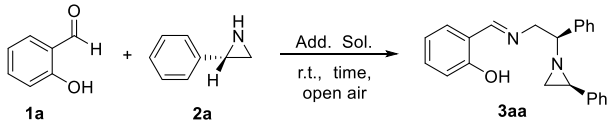
Activated aziridines (with electron-withdrawing substituents on their N atom, such as acyl, sulfonyl, or phosphoryl, etc.) show high activity and easily undergo ring-opening reactions with other reagents, such as various nucleophiles. 2) Unactivated aziridines (with alkyl/aryl substituents on their N atom or without any substituent on their N atom) often require protonic or Lewis acid-activation in their ring-opening reactions (Scheme 1 **B**).[14] The self-ring opening reaction of N-unsubstituted aziridines is an effective way to prepare 1-(2-aminoalkyl)aziridines, which are important intermediates for the synthesis of aziridine-derived chiral imine ligands. However, unfortunately, there are a few reports on this transformation in the literature till now because aziridines are both weak nucleophiles (their N atom) and electrophiles (their carbon atoms).[12,15,16] Generally, the attacked aziridines as nucleophiles should be activated by protonic or Lewis acids, while in the same time, as nucleophiles, the attacking aziridines are also coordinated with the acids, reducing their nucleophilicity. As a result, the reactions occur under unfavorable conditions, such as high temperature, long time, and low yields. Under these conditions, the ring-openings usually occur on the less substituted C-N bonds for unsymmetric aziridines in the limited literature.[12,15] In 1987, Blum and coworkers reported another strategy to achieve the self-ring opening reactions of symmetrical phenanthrene-9,10-imine with aromatic aldehydes in moderate yields (Scheme 1 **C**).[16] This promoted us to develop a new synthetic strategy to direct synthesis of novel chiral tridentate aziridine-containing imine ligands from enantiopure aziridines and salicylaldehydes through a regiospecific and stereospecific iminium-mediated self-ring opening reaction (Scheme 1 **D**). The (*S*)-2-alkylaziridine-derived tridentate ligands displayed exceptionally high activity and stereoselectivity in the asymmetric aldol reactions of acetone with aromatic aldehydes (up to 98% yield and 94% ee).

Results and Discussion

At the outset of this study, salicylaldehyde (**1a**) and (*S*)-2-phenylaziridine (**2a**) were employed as the model substrates to optimize reaction conditions (Table 1). Initially, product **3aa** was obtained in 6% ^{1}H-NMR yield when **2a** was 2.2 equivalents in DCM without any additive under stirring at room temperature for 3 hours (Table 1, entry 1). The structure of product **3aa** was identified by one- and two-dimensional NMR spectra (see SI). The imine hydrogen (at 8.33 ppm) had obvious long-range couplings with the two hydrogens (at 4.04 and 3.97 ppm) of the methylene group in the H-H COSY spectrum of **3aa**, revealing that the carbon next to the imine should be a secondary carbon with two hydrogens (-HC=NCH_2-). It should be clearly seen that the chemical shift of the aliphatic tertiary carbon in the moiety of -HC=NCH_2C**H**(Ph)- was 75.0 ppm by the HSQC spectrum of **3aa**, and the $^3J_{C\text{-}H}$ couplings of three hydrogens on the aziridine and the tertiary carbon were observed in the HMBC spectrum of **3aa**. These results confirmed that the tertiary carbon was directly linked to the nitrogen atom of the aziridine. The stereo configuration was further confirmed by X-ray single crystal diffraction analysis of product **3ca** (Fig. 1).[17] Considering that the removal of water was beneficial to the further formation of the imine during the reaction, anhydrous $MgSO_4$ was added into the reaction system. Unfortunately, the yield was not significantly improved (Table 1, entry 2). Product **3aa** was obtained in 31% yield when 3 Å molecular sieves (MS) were added as dehydrating agents (Table 1, entry 3). The results indicated that the dehydrating agent molecular sieves played a significant role in the reaction. 43% Yield was obtained when the reaction was conducted under Blum's reaction conditions,[16] in the presence of 3 Å molecular sieves in EtOH under reflux for 6 hours (Table 1, entry 4). The yield was improved to 54% by replacement of 3 Å molecular sieves with 4 Å molecular sieves (Table 1, entry 5).

Table 1. Optimization of the reaction conditions[a)]



Entry	**2a** (equiv)	Sol.	Add.	Time (h)	Yield (%)[b)]
1	2.2	DCM	-	3	6
2	2.2	DCM	$MgSO_4$	3	9
3	2.2	DCM	3Å MS	3	31
4[c)]	2.2	EtOH	3Å MS	6	43
5	2.2	DCM	4Å MS	3	54
6	2.2	DCE	4Å MS	3	52
7[c)]	2.2	EtOH	4Å MS	3	49
8	2.2	THF	4Å MS	3	36
9	2.2	MeCN	4Å MS	3	43
10	2.2	toluene	4Å MS	3	65
11	2.2	toluene	4Å MS	6	70
12	2.2	toluene	4Å MS	12	80
13	2.2	toluene	4Å MS	24	82
14	2.0	toluene	4Å MS	12	66
15	**2.5**	**toluene**	**4Å MS**	**12**	**84**
16	2.8	toluene	4Å MS	12	77
17[d)]	2.5	toluene	4Å MS	12	64
18[e)]	2.5	toluene	4Å MS	12	61
19[f)]	2.5	toluene	4Å MS	12	58
20	2.5	xylene	4Å MS	12	65
21	2.5	PhCl	4Å MS	12	82
22	2.5	$PhCF_3$	4Å MS	12	78

[a)] All reactions were conducted on a 0.3 mmol scale of **1a** in the presence of additive (Add.) in 1 mL of solvent (Sol.) under stirring in open air at room temperature (r.t.) unless otherwise indicated. [b)] The yield was determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard. [c)] The reaction was conducted under reflux. [d)] Under N_2 atmosphere. [e)] Isolated yield through silica gel column

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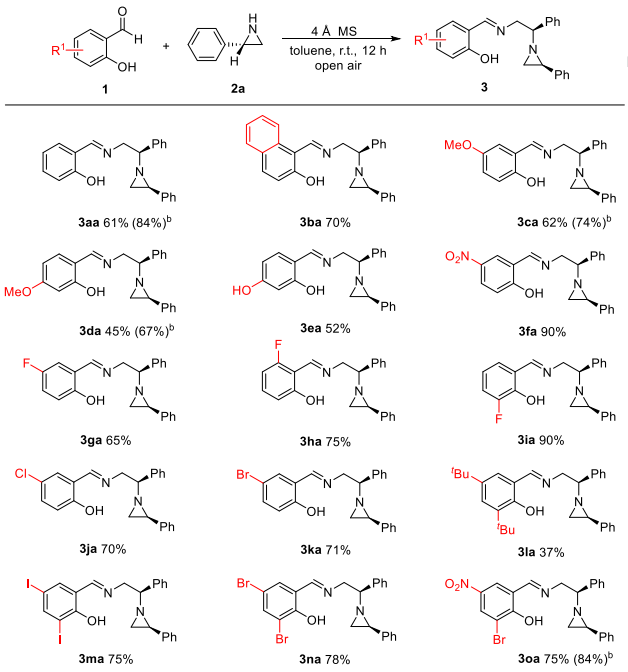
chromatography. [f] Isolated yield through the Et_3N-neutralized silica gel column chromatography.

The results indicated that the 4 Å molecular sieves had better dehydrating effect in the reaction. So 4 Å molecular sieves were used in the subsequent optimizations. A similar yield (52%) was obtained when the reaction was performed in DCE (1,2-dichloroethane) (Table 1, entry 6). The yield deceased from 54% to 49% when the reaction was conducted in refluxing EtOH (Table 1, entry 7). Solvents THF, MeCN, and toluene were then screened and toluene was found to be the best choice (65% yield) (Table 1, entries 5, 6, 8-10). The yield increased obviously from 65% to 70% to 80% with the prolongation of the reaction time from 3 hours to 6 hours to 12 hours, but it did not increase obviously when the reaction time was further prolonged to 24 hours (Table 1, entries 11-13). Thus, 12 hours was selected as the best reaction time. The equivalent of **2a** was further optimized and it was found that the best yield of 84% was realized when **2a** was 2.5 equivalents (Table 1, entries 14-16). The yield decreased to 64% when the reaction was performed under nitrogen (Table 1, entry 17). The results were doubly checked. The higher yields obtained in open air than that under nitrogen were attributed to the trace amount of water, which activated the molecular sieves (*vide post*). Under the current optimal conditions, product **3aa** was separated and purified by silica gel or the triethylamine-neutralized silica gel column chromatography to give isolated yields of 61% and 58%, respectively (Table 1, entries 18 and 19). The results indicated that the silica gel led to partial decomposition of the imine product **3aa** and trimethylamine-neutralization did not inhibit the decomposition. Some aromatic solvents, such as xylene, chlorobenzene, and (trifluoromethyl)benzene, were tried, but the yield was not further improved (Table 1, entries 20-22). The optimum reaction conditions were finally determined as: salicylaldehyde **1a** (0.3 mmol) and aziridine **2a** (0.75 mmol) were stirred in the presence of 4 Å molecular sieves (400 mg) as an additive in toluene at room temperature for 12 hours in open air (Table 1, entry 15).

With the optimal reaction conditions in hand, the reaction scope was then evaluated (Table 2). First, the reactions of different substituted salicylaldehydes **1a**,**c-o** and 2-hydroxy-1-naphthaldehyde (**1b**) with (*S*)-2-phenylaziridine (**2a**) were examined. The salicylaldehyde (**1a**) gave product **3aa** in an isolated yield of 61% (84% ^{1}H-NMR yield) due to its partial decomposition on a silica gel column. Similarly, the reaction of 2-hydroxy-1-naphthaldehyde (**1b**) with **2a** gave product **3ba** in an isolated yield of 70%. Products **3ca**, **3da**, and **3ea** were obtained in moderate to satisfactory yields when the substituents R^1 on salicylaldehydes are methoxy and hydroxyl groups. The product **3fa** achieved an excellent separated yield of 90% when R^1 is a strong electron-withdrawing 5-NO_2 group. We further tested the effect of the substituent F on different positions on the benzene ring. 5-Fluorosalicylaldehyde (**1g**) produced product **3ga** in a relatively low 65% yield, while 6-fluorosalicylaldehyde (**1h**) afforded product **3ha** in a good yield of 75%. However, 3-fluorosalicylaldehyde (**1i**) gave rise to the desired product **3ia** in an excellent yield of 90%. Both 5-chloro- and 5-bromosalicyladehydes (**1j** and **1k**) afforded the corresponding products **3ja** and **3ka** in 70% and 71% yields, respectively, higher than the corresponding 5-fluorosalicylaldehyde (**1g**) did. The results indicated that the electron-withdrawing groups located on the *ortho*- and/or *para*-position(s) of the hydroxyl group in salicylaldehydes reduced the electronic density of the benzene ring, which increased the acidity of their hydroxyl group, resulting in favorable protonation of their aldehyde group. This is benefit for the nucleophilic addition of aziridines to their aldehyde group. On the other hand, the more acidic hydroxyl group is also benefit for stabilizing the imine products through the intramolecular hydrogen bonding.

The reactions of different disubstituted salicylaldehydes **1l-o** with aziridine **2a** are similar to those of monosubstituted ones (Table 2). When the starting material was 3,5-disubstituted salicylaldehyde **1l** with two electron-donating *tert*-butyl groups, the yield of **3ia** rapidly dropped to only 37%. However, the corresponding target products **3ma**, **3na**, and **3oa** were obtained in good yields when the raw materials were 3,5-disubstituted salicylaldehydes **1m-o** with electron-withdrawing Br, I, NO_2 groups.

Table 2. Scope of different salicylaldehydes[a]



[a] All reactions were carried out with **1** (0.30 mmol), **2a** (0.75 mmol, 89.4 mg), and 4 Å MS (400 mg) in toluene (1.0 mL) at r.t. for 12 hrs. The yields are isolated yields by silica gel column chromatography. [b] The yield was determined by ^{1}H NMR analysis with 1,3,5-trimethoxybenzene as an internal standard in parentheses.

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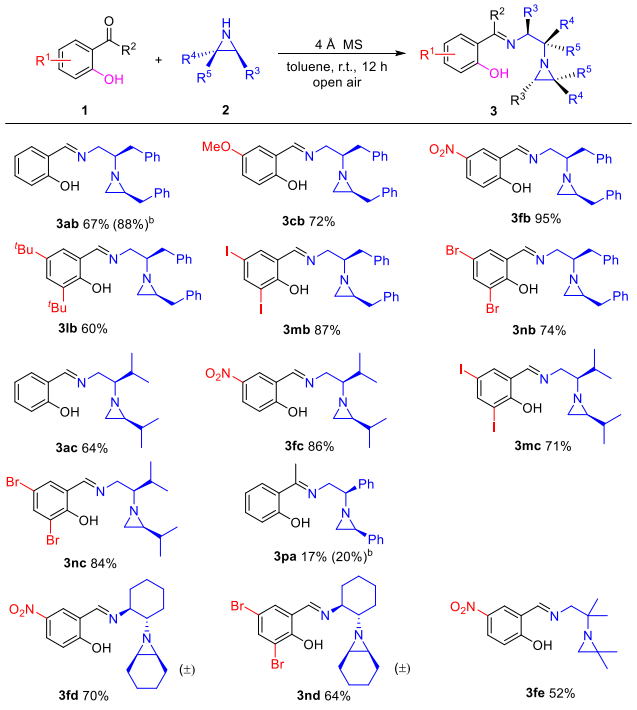
The different aziridines **2** were further attempted (Table 3). Firstly, (*S*)-2-alkylaziridines **2b** and **2c** were reacted with various salicylaldehydes **1**. Both (*S*)-2-benzyl and (*S*)-2-isopropylaziridines (**2b** and **2c**) gave the corresponding desired products **3** in good yields when they reacted with monosubstituted and disubstituted salicylaldehydes **1**. Similarly, the salicylaldehydes with electron-withdrawing substituents tended to produce the corresponding products in better yields than those with electron-donating substituents. It was noteworthy that the ring-opening of (*S*)-2-alkylaziridines **2b** and **2c** also occurred regiospecifically on the more substituted carbon atom with complete inversion of configuration (*vide post*). The reaction of *ortho*-hydroxyacetophenone (**1p**) and (*S*)-2-phenylaziridine (**2a**) was also attempted. The corresponding desired product **3pa** was obtained in a low yield of 17% (isolated yield) and 20% of NMR yield, revealing that the aromatic ketone carbonyl group shows relatively low activity in the reaction.

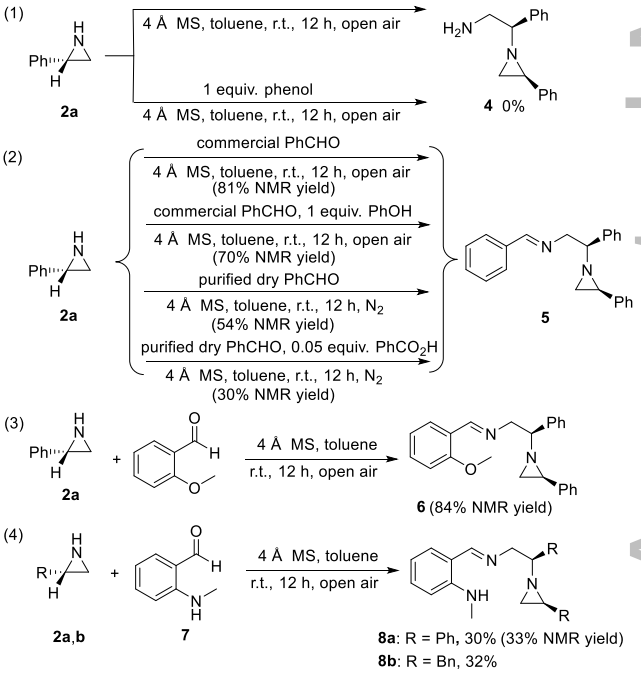
To test the generality of the reaction, the reactions of two representative symmetrical disubstituted aziridines, 1,2-disubstituted aziridine 7-azabicyclo[4.1.0]heptane (**2d**) and 2,2-dimethylaziridine (**2e**), with representative monosubstituted salicylaldehyde **1f** and disubstituted salicylaldehyde **1n** were tried. The corresponding desired products **3fd**, **3nd**, and **3fe** were obtained in moderate to good yields. However, the yields decreased compared to the monosubstituted aziridines.

Table 3. Scope of different aziridines[a)]



a) All reactions were carried out with **1** (0.30 mmol), **2** (0.75 mmol), and 4 Å MS (400 mg) in toluene (1.0 mL) at r.t. for 12 hours. Isolated yield by silica gel column chromatography. b) The yield was determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard in parentheses.

To further explore the reaction mechanism, a series of control experiments was conducted (Scheme 2). First, aziridine **2a** did not undergo the nucleophilic self-ring opening reaction in the presence of 4 Å molecular sieves without or with phenol as an acidic catalyst (Scheme 2, 1), indicating that the additionally added phenolic hydroxyl group did not play a crucial role in the self-ring opening of aziridines. The reaction of the commercial benzaldehyde with aziridine **2a** gave the desired product **5** in 81% ^{1}H-NMR yield. The yield of product **5** dropped to 70% when 1 equivalent of phenol was added. However, the purified dry benzaldehyde yielded product **5** in 54% ^{1}H-NMR yield under nitrogen atmosphere. To verify the effect of benzoic acid generated from the air oxidation of benzaldehyde and possibly existed in benzaldehyde. The reaction of the purified dry benzaldehyde and aziridine **2a** was performed with 5 mol% benzoic acid as an additive under the standard conditions under nitrogen atmosphere. The ^{1}H-NMR yield dropped sharply to 30% (Scheme 2, 2). The results indicated that the catalytic amount of benzoic acid did not promote the reaction, but decreased the yield. The results from the optimization and control experiments revealed that a trace amount of water promoted the reaction possibly because trace water could activate molecular sieves.



Scheme 2. Control experiments.

Furthermore, to test the function of the intramolecular phenolic hydroxyl group, the reaction of *ortho*-methoxybenzaldehyde and aziridine **2a** was performed, giving rise to the desired product **6** in a

good 84% ^{1}H-NMR yield under standard conditions (Scheme 2, 3). The reactions of 2-methylaminobenzaldehyde (**7**) with aziridines **2a** and **2b** were carried out under standard conditions. As expected, the corresponding products **8a** and **8b** were obtained in the isolated yields of 30% (33% ^{1}H-NMR yield) and 32%, respectively, due to the existence of the intramolecular hydrogen bonding between the N-H group and the imine nitrogen atom (Scheme 2, 4). The characteristic peaks of their aliphatic and imine parts in their ^{1}H-NMR spectra verified their existence in their reaction mixtures (see SI). However, unfortunately, products **5** and **6** were not isolated and decomposed completely on silica gel TLC plate or column chromatography.

From the above experiments, first, it should be confirmed that the aziridines did not undergo a self-ring opening reaction by themselves in the presence of molecular seives, even under the catalysis of the intermolecularly phenolic hydroxyl group. However, salicylaldehyde with an intramolecular hydrogen bond promoted the self-ring opening of aziridines slightly (Table 1, entry 1). 4Å molecular sieves accelerated the reaction significantly through iminium intermediates generated from salicylahydehydes and one molecule of aziridines. The intramolecular *ortho*-phenolic hydroxyl group slightly activated the carbonyl group in the formation of iminium intermediates through the intramolecular hydrogen bonding between the hydroxyl group and the carbonyl group, but it played an important role in stabilizing the products through the intramolecular hydrogen bond between the hydroxyl group and the imine nitrogen atom. The existence of the intramolecular hydrogen bond was proved by the chemical shift at 15 ppm of the phenolic hydrogen in products **3** in their proton NMR spectra and in the crystal structure of **3ca** (Fig. 1)[17]. The interatomic distances between the hydrogen atom of the hydroxyl group with the imine nitrogen atom and the aziridine nitrogen atom were 1.873 Å and 3.997 Å, respectively. The results indicated that the intramolecular hydrogen bond existed only between the hydrogen atom of the hydroxyl group and the imine nitrogen atom. On the other hand, aziridines underwent the self-ring opening with complete inversion of the configuration. Therefore, it can be inferred that the reaction mechanism was not the first generation of 1,2-diamines **4** followed by the formation of imines through a nucleophilic addition-dehydration of the carbonyl group of benzaldehydes or acetophenones and diamines **4**.

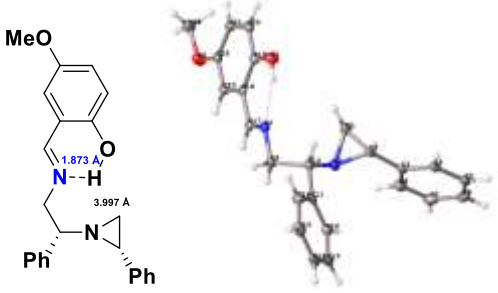
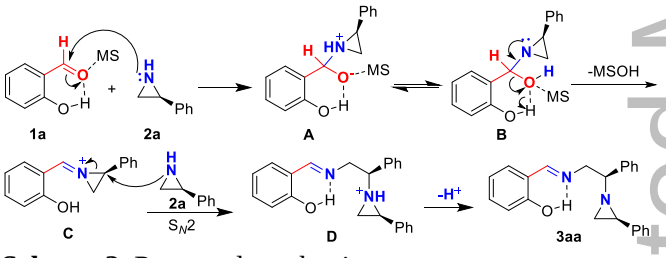


Figure 1. Single crystal structure of **3ca**.

On the basis of the above information, we proposed the following mechanism for the formation of our tridentate chiral imine ligands **3**. The reaction of salicylaldehyde **1a** and (*S*)-2-phenylaziridine **2a** was selected as an example to illustrate the proposed mechanism (Scheme 3). First, 4Å molecular sieves (MS) coordinate with the partially protonated carbonyl group in salicylaldehyde through an intramolecular hydrogen bond, activating the carbonyl group. The nitrogen atom in aziridine **2a** nucleophilically attacks the activated carbonyl group in salicylaldehyde **1a** to form intermediate **A**. A proton transfer gives rise to intermediate **B**, which undergoes an elimination of MS-OH to generate iminium intermediate **C**. The formation of the iminium group increases the electrophilicity of the aziridine ring. Another molecule of aziridine **2a** nucleophilically attacks the more substituted carbon atom of the aziridinium ring through a S_N2 pathway followed by the formation of an intramolecular hydrogen bond to give rise to ring opening intermediate **D**, which loses a proton to afford product **3aa**. The intramolecular hydrogen bond exists in a six-membered ring, stabilizing the products. The aziridinium ring is similar to protonated or Lewis acid-coordinated aziridines, showing similar regioselectivity as protonated or Lewis acid-coordinated aziridines.[18]



Scheme 3. Proposed mechanism.

To verify the proposed reaction mechanism and the optical purities of the synthesized ligands **3**, the enantiomeric excess values of 14 selected representative chiral ligands **3ba**, **3ca**, **3ea**, **3ab**, **3cb**, **3fb**, **3lb**, **3mb**, **3ac**, **3fc**, **3mc**, **3nc**, **8a** and **8b** in Table 4 were determined. The results indicated that all determined chiral ligands were enantiopure with > 99 ee, supporting our proposed mechanism.

The aldol condensation is one of the basic model reactions in organic synthesis and has been commonly used for testing the catalytic activity of newly developed chiral ligands.[19] Therefore, the aldol condensations of aromatic aldehydes and acetone were used to evaluate our synthesized ligands under the catalysis of Lewis acid $Zn(OTf)_2$.

First, the reaction of 4-nitrobenzaldehyde (**9a**) and acetone was conducted without any ligand, affording the desired product in a low yield of 24% (Table 4, entry 1). Different types of chiral ligands **3** and **8** were screened. Unfortunately, the tridentate

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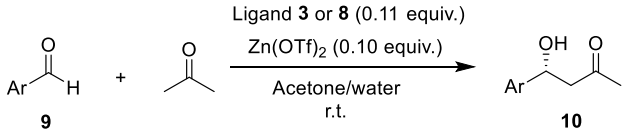
ligands prepared from (*S*)-2-phenylaziridine (**2a**) did not show any efficiency in the stereochemical control with moderate yields. Some representative examples are summarized in Table 4 (entries 2-6). However, the ligands derived from aziridines **2b** and **2c** showed good to excellent yields (63%-98%) and stereoselectivity (73-94% ee) (Table 4, entries 7-13 and 15-18). The ligand **8b** itself can catalyze the reaction. But, it showed low efficiency and stereoselectivity without $Zn(OTf)_2$ (Table 4, entry 14). The results indicated that the ligands with sterically hindered isopropyl group generally are excellent ligands, showing excellent yields (86-98%) and enantioselectivity (85-94% ee) (Table 4, entries 15-18). The chiral ligand **3mc** generated from 3,5-diiodosalicylaldehyde (**1m**) and (*S*)-2-isopropylaziridine (**2c**) was the most excellent one in the asymmetric control (94% ee) with a perfect yield (90%) (Table 4, entry 18). However, chiral ligands **3ac** and **3fc** derived from salicylaldehyde (**1a**) and 5-nitrosalicylaldehyde (**1f**) with (*S*)-2-isopropylaziridine (**2c**) showed the highest reactivity (98% yield) with excellent enantioselectivities (89% and 91% ee, respectively).

Table 4. Aldol condensation of aromatic aldehydes and acetone catalyzed by $Zn(OTf)_2$-tridentate chiral ligands **3** and **8**[a)]



a: Ar = 4-$NO_2C_6H_4$, **b**: Ar = 3-$NO_2C_6H_4$, **c:** Ar = 2-$NO_2C_6H_4$, **d**: Ar = 4-NCC_6H_4, **e:** Ar = 4-ClC_6H_4, **f**: Ar = 4-BrC_6H_4, **g:** Ar = 3-$MeOC_6H_4$, **h**: Ar = 2-naphthyl

Entry	Ligand	ee. (%) [b)] of Ligand	**10**	Time (h)	Yield (%)[c)]	ee. (%) [b)] of **10**
1	**--**	-	**10a**	58	24	-
2	**3ba**	>99	**10a**	118	60	0
3	**3ca**	>99	**10a**	104	72	0
4	**3ea**	>99	**10a**	28	49	0
5	**3oa**	-[d)]	**10a**	28	54	-8
6	**8a**	>99	**10a**	45	40	0
7	**3ab**	>99	**10a**	36	87	80
8	**3cb**	>99	**10a**	36	73	78
9	**3fb**	>99	**10a**	36	79	74
10	**3lb**	>99	**10a**	31	63	73
11	**3mb**	>99	**10a**	36	80	88
12	**8b**	>99	**10a**	28	76	75
13	**8b**		**10a**	52	82	73
14	**8b**		**10a**	52	19	-5[e)]
15	**3ac**	>99	**10a**	34	98	89
16	**3fc**	>99	**10a**	34	98	91
17	**3nc**	>99	**10a**	36	86	85
18	**3mc**	>99	**10a**	36	90	94
19	**3mc**		**10b**	36	86	78
20	**3mc**		**10c**	36	95	81
21	**3mc**		**10d**	36	85	75
22	**3mc**		**10e**	36	80	77
23	**3mc**		**10f**	36	82	83
24	**3mc**		**10g**	48	69	81
25	**3mc**		**10h**	48	74	81

[a)] All reactions were carried out with aldehyde (0.50 mmol), ligand (0.055 mmol), $Zn(OTf)_2$ (18.2 mg, 0.05 mmol) in 2 mL of acetone/H_2O mixture (9:1, v/v) at r.t. The absolute configuration was assigned as (*R*) by comparison of the specific rotations with those of the known compounds.[19] [b)] Determined by HPLC analysis using a Phenomenex Lux 5μ Cellulose-1 or Daicel Chiralpak AS-H/AD-H column with *i*-PrOH/hexane as eluent. [c)] Isolated yields by column chromatography on silica gel. [d)] Poor solubility made it unable to be detected. [e)] Without $Zn(OTf)_2$.

Different aromatic aldehydes **9** were further evaluated under the catalysis of $Zn(OTf)_2$ and ligand **3mc** in acetone. Products **10b-f** achieved good to excellent yields of 80-95% when Ar with electron-withdrawing groups (Table 4, entries 19-23). Both 3-methoxybenzaldehyde (**9g**) and 2-naphthaldehyde (**9h**) afforded the corresponding products **10g** and **10h** in 69% and 74% yields, respectively (Table 4, entries 24 and 25). The chiral ligand **3mc** exhibited good asymmetric control to afford products **10b-10h** with good enantioselectivities (75-83% ee). The results indicated that the novel aziridine-containing tridentate chiral ligands derived from salicylaldehydes and (*S*)-2-isopropylaziridine are highly efficient in the $Zn(OTf)_2$-catalyzed asymmetric aldol reaction of aromatic aldehydes and acetone with good to excellent stereoselectivity.

Conclusion

In summary, we developed a simple and efficient method for the direct synthesis of optically active aziridine-containing tridentate imine ligands. The method achieved the regiospecific cleavage of more substituted C-N bonds of aziridines through an iminium-mediated self-ring opening reaction of aziridines with up to 95% yield and complete inversion of configuration. This method has the advantage of easy availability of starting materials as well. The tridentate ligands derived from 2-alkylaziridines displayed good to excellent activity and stereoselectivity in the $Zn(OTf)_2$-catalyzed asymmetric aldol reaction of acetone and aromatic aldehydes.

Experimental Section

General Information. Unless otherwise noted, all materials were purchased from commercial suppliers without further purification. 4 Å Molecular sieves were activated for 3 hours using a muffle furnace at 580 °C. Toluene was refluxed over Na with benzophenone as an indicator and freshly distilled prior to use. Commercially available benzaldehyde was washed with saturated sodium hydrogen carbonate, dried over anhydrous sodium sulfate, distilled and then kept under nitrogen atmosphere. Flash

column chromatography was performed using silica gel (normal phase, 200-300 mesh) from Branch of Qingdao Haiyang Chemical. Petroleum ether (PE) used for column chromatography is 60–90 ºC fraction, and the removal of residue solvent was accomplished under rotovap. Reactions were monitored by thin-layer chromatography on silica gel GF254 coated 0.2 mm plates from Institute of Yantai Chemical Industry. The plates were visualized under UV light, as well as other TLC stains. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker 400 MHz spectrometer in $CDCl_3$, DMSO-d_6, or acetone-d_6 with solvent peaks as internal standards, and the chemical shifts (δ) are reported in parts per million (ppm). All coupling constants (J) in ^{1}H NMR are absolute values given in hertz (Hz) with peaks labeled as single (s), broad singlet (brs), doublet (d), triplet (t), quartet (q), and multiplet (m). The IR spectra (KBr pellets, ν [cm^{-1}]) were taken on a Bruker Tensor 27 FTIR spectrometer. HRMS measurements were carried out on an Agilent LC/MSD TOF mass spectrometer. Melting points were obtained on a Yanaco MP-500 melting point apparatus and are uncorrected. Single crystal X-ray diffraction analysis (**3ca**) was performed on an Agilent Gemini E single crystal X-ray diffractometer. Specific rotations were measured on an Anton Paar MCP500 polarimeter. The enantiomeric excesses were determined by chiral HPLC analysis using an Agilent 1260 LC instrument with Phenomenex Lux 5μ Cellulose-1 or Daicel Chiralpak AS-H/AD-H column with a mixture of isopropyl alcohol and hexane as eluents.

General procedures for the synthesis of aziridines 2

Preparation of **2a**, **2b**, and **2d**:[20] Amino primary alcohol (30 mmol) was dissolved in acetonitrile (100 mL) in an 250 mL round-bottom flask, and the reaction mixture was cooled to 0 °C followed by dropwise addition of chlorosulfonic acid (4.19 g, 2.37 mL, 36 mmol). The resulting heterogeneous solution was stirred constantly at room temperature for 6 h. The reaction mixture was then filtered under vacuum followed by washing with ethyl acetate. The filter cake was dried in air under infrared light to afford the aminosulfate salt as colorless solid.

Aminosulfate salt was dissolved in NaOH (50 mL, aq. 6 mol/L) followed by addition of toluene (50 mL). The resulting biphasic solution was heated under reflux for 18 h with constant stirring. Then, the solution was extracted with ethyl acetate. The combined organic phase was dried over anhydrous $NaSO_4$ and evaporated under reduced pressure followed by purification by column chromatography on the Et_3N-pretreated silica gel, affording aziridine **2a**, **2b**, or **2d**.

(*S*)-2-Phenylaziridine (**2a**):[20] With (*S*)-2-amino-2-phenylethan-1-ol as materials. 2.33 g, yield 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H), 7.20 (t, J = 6.3 Hz, 3H), 2.94 (dd, J = 5.3, 3.4 Hz, 1H), 2.13 (d, J = 6.0 Hz, 1H), 1.73 (s, 1H), 0.75 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 128.5, 127.0, 125.7, 77.6, 77.3, 77.0, 32.0, 29.4.

(*S*)-2-Benzylaziridine (**2b**):[20] With (*S*)-2-amino-3-phenylpropan-1-ol as materials. 2.30 g, yield 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.06 (m, 5H), 2.64 (dd, J = 14.4, 6.1 Hz, 1H), 2.51 (dd, J = 14.4, 5.9 Hz, 1H), 2.03 (qd, J = 5.9, 3.5 Hz, 1H), 1.64 (d, J = 5.8 Hz, 1H), 1.29 (d, J = 3.5 Hz, 1H), 0.18 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 128.8, 128.4, 126.3, 40.1, 30.9, 24.8.

7-Azabicyclo[4.1.0]heptane (**2d**):[20] With *trans*-2-aminocyclohexan-1-ol as materials. 1.05 g, yield 36%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 – 2.14 (m, 2H), 1.84 – 1.78 (m, 4H), 1.41 – 1.29 (m, 2H), 1.27 – 1.17 (m, 2H), 0.68 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.3, 24.6, 20.1.

Preparation of **2c** and **2e**:[21] Vicinal amino alcohol (30 mmol) was dissolved in diethyl ether (100 mL) in a 250 mL round-bottom flask. After the amino alcohol was dissolved completely, and the reaction mixture was cooled to 0 °C followed by dropwise addition of chlorosulfonic acid (4.19 g, 2.37 mL, 36 mmol). The resulting heterogeneous solution was stirred constantly at room temperature for 6 hours. The reaction mixture was then filtered under vacuum followed by washing with diethyl ether. The filter cake was dried in air under infrared light to afford the aminosulfate salt as colorless solid.

Aminosulfate salt was dissolved in NaOH (50 mL, aq. 6 mol/L) in a 100 mL round-bottom flask, and the mixture was stirred at r.t. overnight, and then steam-distilled. The distillate was saturated with KOH pellets and the upper organic layer, which was separated, was extracted with Et_2O (3 × 20 mL), dried over anhydrous $NaSO_4$ and concentrated under reduced pressure, giving products **2c** and **2e** as colorless oil.

(*S*)-2-Isopropylaziridine (**2c**):[21] With (*S*)-2-amino-3-methylbutan-1-ol as materials. 2.08 g, yield 61%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 – 1.37 (m, 2H), 1.06 (s, 1H), 0.89 – 0.79 (m, 1H), 0.75 (d, J = 6.3 Hz, 3H), 0.69 (d, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 36.7, 32.6, 23.8, 20.2, 19.5.

2,2-Dimethylaziridine (**2e**):[21] With 2-amino-2-methylpropan-1-ol as materials. 1.21 g, yield 57%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 2 H), 1.55 (s, 1 H), 1.01 (s, 6 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 32.9, 30.5, 24.3.

Procedure for the synthesis of 2-(methylamino)benzaldehyde (7)[22]

Quinoline (20 mmol, 2.58 g, 2.37 mL), methyl iodide (24 mmol, 3.41 g, 1.49 mL), and 20 mL of dry THF were added into a 100 mL dry three-necked flask equipped with a condensor under a nitrogen atmosphere. The resulting solution was refluxed for 2 hours. The reaction mixture was allowed to cool to room temperature and an excess of aqueous dimethylamine was added, then mixture was evaporated under reduced pressure to afford crude product of 1-methylquinolinium salt.

Potassium hydroxide (200 mmol, 11.22 g), 33% hydrogen peroxide solution (25 mL), 1,2-dichloroethane (40 mL), and water (40 mL) were added into a 250 mL round-bottomed flask at 0 °C. A solution of crude 1-methylquinolinium salt in 20 mL of water was slowly added into the reaction system. The resulting solution was stirred at room temperature for 48 hours. Then, the solution was extracted with dichloromethane (3×20 mL), washed with saturated sodium sulfite, dried over anhydrous $NaSO_4$, and evaporated in vacuo. The crude residue was purified by column chromatography (silica gel, petroleum ether:ethyl acetate 15:1, *v/v*) to give product **7** as yellow oil. 1.73 g, yield 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.49 – 7.37 (m, 2H), 6.73 – 6.63 (m, 2H), 3.48 (s, 1H), 2.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 151.4, 136.5, 135.7, 118.3, 114.7, 110.3, 29.0.

General procedure for the synthesis of ligands 3 and 8

Activated 4 Å molecular sieves (about 400 mg) were added in toluene (1.0 mL) in a 10 mL reaction tube equipped with a magnetic stirring bar. Then benzaldehyde or acetophenone **1** or **7** (0.3 mmol) and aziridine **2** (0.75 mmol) were added. The resulting solution was stirred at room temperature for 12 hours in open air. After completion of the reaction, resulting mixture was filtered, and the filtrate was evaporated in vacuo to remove the volatile materials. The crude residue was purified by column chromatography (silica gel, petroleum ether:ethyl acetate) to give product **3** or **8** as yellow solid or oil.

2-((*E*)-(((*R*)-2-Phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3aa)

10.1002/adsc.201801545

Yellow solid, 62 mg, yield 61%, m.p. 99–100 °C, R_f = 0.5 (PE/EA = 5:1, *v*/*v*), $[\alpha]_D^{25}$ = +56.0 (c 1.00, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.43 (s, 1H), 8.33 (s, 1H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.35 – 7.27 (m, 3H), 7.25 – 7.21 (m, 4H), 7.19 – 7.13 (m, 3H), 6.98 (d, *J* = 8.3 Hz, 1H), 6.88 (t, *J* = 7.4 Hz, 1H), 4.04 (dd, *J* = 12.1, 7.3 Hz, 1H), 3.97 (dd, *J* = 12.1, 5.2 Hz, 1H), 3.04 (t, *J* = 6.3 Hz, 1H), 2.41 (dd, *J* = 6.3, 3.5 Hz, 1H), 2.11 (d, *J* = 3.3 Hz, 1H), 2.01 (d, *J* = 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 161.2, 141.1, 139.8, 132.3, 131.4, 128.4, 128.1, 127.5, 127.5, 126.7, 126.4, 118.8, 118.6, 117.0, 75.0, 66.9, 39.2, 38.9. IR (KBr) *v* 3061, 3030, 2924, 2851, 1637, 1592, 1492, 1463, 1267, 1037, 785, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{23}N_2O^+$ $[M+H]^+$: 343.1805, found 343.1811.

1-((*E*)-(((*R*)-2-Phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)naphthalen-2-ol (3ba)
Yellow solid, 72 mg, yield 70%, m.p. 140–142 °C, R_f = 0.2 (PE/EA = 2:1, *v*/*v*), $[\alpha]_D^{25}$ = -24.5 (c 1.08, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.55 (s, 1H), 8.67 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 9.3 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.39 (m, 3H), 7.34 – 7.27 (m, 3H), 7.27 – 7.23 (m, 3H), 7.22 – 7.16 (m, 3H), 6.97 (d, *J* = 9.3 Hz, 1H), 4.05 – 3.93 (m, 2H), 3.04 (t, *J* = 6.0 Hz, 1H), 2.45 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.18 (d, *J* = 3.5 Hz, 1H), 2.03 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 159.0, 140.0, 139.5, 137.2, 133.8, 129.2, 128.7, 128.2, 128.0, 127.5, 126.9, 126.3, 124.8, 122.8, 118.0, 106.8, 74.7, 60.4, 39.4, 39.0. IR (KBr) *v* 3059, 3030, 2956, 2925, 2853, 1629, 1544, 1494, 1449, 1354, 1207, 834, 747, 670 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{27}H_{25}N_2O^+$ $[M+H]^+$: 393.1961, found 393.1966. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 10:90, *v*/*v*, 1.0 mL/min, 254 nm), t_R = 24.75 min, ee > 99%.

4-Methoxy-2-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3ca)
Yellow crystals, 69 mg, yield 62%, m.p. 134–135 °C, R_f = 0.4 (PE/EA = 5:1, *v*/*v*), $[\alpha]_D^{25}$ = +60.4 (c 1.00, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.89 (s, 1H), 8.28 (s, 1H), 7.39 (d, *J* = 7.0 Hz, 2H), 7.31 – 7.20 (m, 5H), 7.19 – 7.12 (m, 3H), 6.95 – 6.87 (m, 2H), 6.74 (s, 1H), 4.09 – 3.93 (m, 2H), 3.77 (s, 3H), 3.03 (t, *J* = 5.9 Hz, 1H), 2.40 (d, *J* = 2.1 Hz, 1H), 2.10 (d, *J* = 2.4 Hz, 1H), 2.00 (d, *J* = 6.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 155.3, 152.0, 141.1, 139.9, 128.4, 128.2, 127.5, 126.8, 126.4, 119.3, 118.5, 117.7, 115.0, 75.0, 67.1, 56.0, 39.3, 39.0. IR (KBr) *v* 3060, 3029, 2955, 2925, 2851, 1637, 1592, 1492, 1270, 1037, 784, 748, 699 cm^{-1}.HRMS-ESI (*m/z*): calcd for $C_{24}H_{25}N_2O_2^+$ $[M+H]^+$: 373.1911, found 373.1916. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 10:90, *v*/*v*, 1.0 mL/min, 254 nm), t_R = 10.17 min, ee > 99%.

5-Methoxy-2-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3da)
Yellow solid, 50 mg, yield 45%, m.p. 82–85 °C, R_f = 0.5 (PE/EA = 1:1, *v*/*v*), $[\alpha]_D^{25}$ = -34.4 (c 1.14, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.93 (s, 1H), 8.12 (s, 1H), 7.37 (d, *J* = 7.0 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 2H), 7.24 – 7.19 (m, 3H), 7.19 – 7.12 (m, 3H), 7.06 (d, *J* = 8.6 Hz, 1H), 6.44 (d, *J* = 2.2 Hz, 1H), 6.37 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.95 (dd, *J* = 12.2, 7.2 Hz, 1H), 3.88 (dd, *J* = 12.3, 5.3 Hz, 1H), 3.79 (s, 3H), 2.99 (t,*J* = 6.8 Hz, 1H), 2.39 (dd, *J* = 6.4, 3.5 Hz, 1H), 2.10 (d, *J* = 3.4 Hz, 1H), 1.99 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 165.0, 163.8, 141.0, 139.9, 132.8, 128.4, 128.2, 127.6, 127.5, 126.8, 126.4, 112.3, 106.5, 101.4, 75.0, 65.3, 55.4, 39.3, 38.9. IR (KBr) *v* 3061, 3030, 2957, 2925, 2852, 1626, 1513, 1494, 1452, 1225, 1135, 837, 747, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{24}H_{25}N_2O_2^+$ $[M+H]^+$: 373.1911, found 373.1917.

4-((*E*)-(((*R*)-2-Phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)benzene-1,3-diol (3ea)
Yellow solid, 56 mg, yield 52%, m.p. 135–136 °C, R_f = 0.3 (PE/EA = 1:1, *v*/*v*), $[\alpha]_D^{25}$ = -28.7 (c 1.00, dichloromethane). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.72 (s, 1H), 10.01 (s, 1H), 8.26 (s, 1H), 7.39 – 7.31 (m, 2H), 7.24 – 7.16 (m, 5H), 7.16 – 7.09 (m, 4H), 6.23 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.16 (d, *J* = 2.2 Hz, 1H), 3.89 (dd, *J* = 12.7, 6.1 Hz, 1H), 3.83 (dd, *J* = 12.8, 5.7 Hz, 1H), 3.01 (t, *J* = 6.0 Hz, 1H), 2.44 (dd, *J* = 6.4, 3.3 Hz, 1H), 2.03 (d, *J* = 6.7 Hz, 1H), 1.91 (d, *J* = 3.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.1, 165.6, 162.4, 141.9, 140.8, 133.9, 128.6, 128.5, 127.9, 127.6, 127.0, 126.4, 111.7, 107.3, 103.2, 74.0, 64.0, 39.3, 39.0. IR (KBr) *v* 3060, 3031, 2956, 2925, 2854, 2610, 1634, 1464, 1366, 1226, 1119, 848, 795, 742, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{23}N_2O_2^+$ $[M+H]^+$: 359.1754, found 359.1758. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 10:90, *v*/*v*, 1.0 mL/min, 215 nm), t_R = 28.70 min, ee > 99%.

4-Nitro-2-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3fa)
Yellow oil, 105 mg, yield 90%, R_f = 0.5 (PE/EA = 1:1, *v*/*v*), $[\alpha]_D^{25}$ = -34.2 (c 1.05, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.73 (s, 1H), 8.25 (s, 1H), 8.19 – 8.14 (m, 2H), 7.36 (dd, *J* = 7.8, 1.3 Hz, 2H), 7.31 – 7.27 (m, 1H), 7.27 – 7.24 (m, 2H), 7.24 – 7.21 (m, 2H), 7.21 – 7.13 (m, 3H), 6.95 (d, *J* = 10.0 Hz, 1H), 4.10 – 3.98 (m, 2H), 3.06 (t, *J* = 5.9 Hz, 1H), 2.45 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.10 (d, *J* = 3.5 Hz, 1H), 1.97 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 165.3, 140.0, 139.5, 138.6, 128.6, 128.5, 128.4, 128.3, 128.0, 127.5, 127.0, 126.3, 119.4, 116.6, 74.3, 64.5, 39.3, 39.2. IR (KBr) *v* 3061, 3031, 2960, 2924, 2853, 1640, 1613, 1544, 1492, 1450, 1337, 1227, 1027, 834, 800, 752, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{22}N_3O_3^+$ $[M+H]^+$: 388.1656, found 388.1658.

4-Fluoro-2-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3ga)
Yellow solid, 70 mg, yield 65%, m.p. 122–125 °C, R_f = 0.5 (PE/EA = 5:1, *v*/*v*), $[\alpha]_D^{25}$ = +59.5 (c 0.92, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.15 (s, 1H), 8.26 (s, 1H), 7.42 – 7.37 (m, 2H), 7.32 – 7.27 (m, 2H), 7.26 – 7.18 (m, 4H), 7.16 (dd, *J* = 6.5, 4.9 Hz, 2H), 7.08 – 7.01 (m, 1H), 6.96 – 6.90 (m, 2H), 4.09 – 3.95 (m, 2H), 3.05 (dd, *J* = 6.9, 5.7 Hz, 1H), 2.42 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.10 (d, *J* = 3.5 Hz, 1H), 2.00 (d, *J* = 6.6 Hz, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2 (d, $J_{C\text{-}F}$ = 2.7 Hz), 157.3 (d, $J_{C\text{-}F}$ = 1.5 Hz), 155.4 (d, $J_{C\text{-}F}$ = 236.5 Hz), 140.9, 139.8, 128.4 , 128.2, 127.6, 127.5, 126.8, 126.4, 119.3 (d, $J_{C\text{-}F}$ = 23.2 Hz), 118.5 (d, $J_{C\text{-}F}$ = 7.2 Hz), 118.0 (d, $J_{C\text{-}F}$ = 7.3 Hz), 116.4 (d, $J_{C\text{-}F}$ = 23.1 Hz), 74.9, 66.9, 39.2, 39.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -126.0. IR (KBr) *v* 3061, 3030, 2957, 2925, 2853, 1638, 1588, 1491, 1375, 1273, 1254, 1143, 1090, 1027, 865, 819, 784, 746, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{22}FN_2O^+$ $[M+H]^+$: 361.1711, found 361.1710

3-Fluoro-2-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3ha)
Yellow solid, 81 mg, yield 75%, m.p. 51–53 °C, R_f = 0.5 (PE/EA = 1:1, *v*/*v*), $[\alpha]_D^{25}$ = +63.7 (c 0.67, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.98 (s, 1H), 8.65 (s, 1H), 7.38 (d, *J* = 6.9 Hz, 2H), 7.31 – 7.26 (m, 2H), 7.26 – 7.20 (m, 4H), 7.19 – 7.14 (m, 3H), 6.73 (d, *J* = 8.5 Hz, 1H), 6.51 (dd, *J* = 9.5, 8.7 Hz, 1H), 4.10 – 3.93 (m, 2H), 3.06 – 2.96 (m, 1H), 2.41 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.10 (d, *J* = 3.5 Hz, 1H), 1.98 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3 (d, $J_{C\text{-}F}$ = 4.2 Hz), 162.8 (d, $J_{C\text{-}F}$ = 248.5 Hz), 160.2 (d, $J_{C\text{-}F}$ = 7.3 Hz), 140.9, 139.8, 133.3 (d, $J_{C\text{-}F}$ = 11.3 Hz), 128.5, 128.2, 127.6, 127.5, 126.8, 126.4, 113.3 (d, $J_{C\text{-}F}$ = 2.7 Hz), 107.9 (d, $J_{C\text{-}F}$ = 12.4 Hz), 104.4 (d, $J_{C\text{-}F}$ = 20.8 Hz), 75.0, 66.7, 39.3, 39.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -122.0. IR (KBr) *v* 3062, 3030, 2956, 2925, 2853, 1634, 1586, 1495, 1462, 1378, 1236, 1203, 1011, 851, 787, 745, 724, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{22}FN_2O^+$ $[M+H]^+$: 361.1711, found 361.1712.

2-Fluoro-6-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3ia)
Yellow oil, 97 mg, yield 90%, R_f = 0.3 (PE/EA = 5:1, *v*/*v*), $[\alpha]_D^{25}$ = +47.3 (c 0.62, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.85 (s, 1H), 8.31 (d, *J* = 0.7 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.31 – 7.26 (m, 2H), 7.26 – 7.21 (m,

3H), 7.21 – 7.11 (m, 4H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.77 (td, *J* = 7.9, 4.5 Hz, 1H), 4.15 – 3.88 (m, 2H), 3.14 – 2.98 (m, 1H), 2.43 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.12 (d, *J* = 3.5 Hz, 1H), 2.01 (d, *J* = 6.6 Hz, 1H).^{13}C NMR (101 MHz, $CDCl_3$) *δ* 165.90 (d, J_{C-F} = 2.2 Hz), 152.8, 150.8 (d, J_{C-F} = 13.1 Hz), 150.3, 140.8, 139.7, 128.5, 128.2, 127.7, 127.5, 126.8, 126.4, 120.3 (d, J_{C-F} = 4.1 Hz), 118.6 (d, J_{C-F} = 17.8 Hz), 117.6 (d, J_{C-F} = 6.6 Hz), 74.8, 66.3, 39.3, 39.0. ^{19}F NMR (376 MHz, $CDCl_3$) *δ* -137.9. IR (KBr) *ν* 3062, 3030, 2956, 2925, 2853, 1637, 1467, 1378, 1276, 1250, 1089, 1027, 847, 749, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{22}FN_2O^+$ $[M+H]^+$: 361.1711, found 361.1713.

4-Chloro-2-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3ja)
Yellow solid, 79 mg, yield 70%, m.p. 125–127 °C, R_f = 0.5 (PE/EA = 5:1, *v/v*), $[\alpha]_D^{25}$ = +36.8 (c 0.94, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 13.42 (s, 1H), 8.25 (s, 1H), 7.42 – 7.36 (m, 2H), 7.32 – 7.28 (m, 2H), 7.28 – 7.22 (m, 4H), 7.20 (dd, *J* = 4.7, 2.1 Hz, 2H), 7.17 – 7.14 (m, 2H), 6.92 (d, *J* = 8.8 Hz, 1H), 4.08 – 3.95 (m, 2H), 3.04 (dd, *J* = 6.7, 5.9 Hz, 1H), 2.42 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.10 (d, *J* = 3.5 Hz, 1H), 1.99 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 165.1, 159.9, 140.9, 139.8, 132.2, 130.5, 128.4, 128.2, 127.6, 127.5, 126.8, 126.4, 123.2, 119.5, 118.7, 74.9, 66.8, 39.3, 39.0. IR (KBr) *ν* 3061, 3030, 2957, 2924, 2853, 1634, 1576, 1479, 1378, 1278, 1202, 1090, 1026, 820, 745, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{22}ClN_2O^+$ $[M+H]^+$: 377.1415, found 377.1416.

4-Bromo-2-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3ka)
Yellow crystals, 99 mg, yield 71%, m.p. 118–120 °C, R_f = 0.5 (PE/EA = 5:1, *v/v*), $[\alpha]_D^{25}$ = +22.7 (c 1.13, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 13.44 (s, 1H), 8.21 (s, 1H), 7.39 – 7.34 (m, 3H), 7.32 – 7.25 (m, 3H), 7.24 – 7.20 (m, 3H), 7.19 – 7.12 (m, 3H), 6.86 (d, *J* = 8.8 Hz, 1H), 4.10 – 3.87 (m, 2H), 3.12 – 2.94 (m, 1H), 2.40 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.08 (d, *J* = 3.5 Hz, 1H), 1.96 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 165.0, 160.4, 140.9, 139.8, 135.0, 133.5, 128.5, 128.2, 127.7, 127.5, 126.8, 126.4, 120.2, 119.1, 110.0, 74.9, 66.8, 39.3, 39.00. IR (KBr) *ν* 3061, 3029, 2957, 2925, 2853, 1634, 1476, 1366, 1277, 1202, 1088, 1027, 820, 750, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{22}BrN_2O^+$ $[M+H]^+$: 421.0910, found 421.0912.

2,4-Di-*tert*-butyl-6-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3la)
Yellow oil, 50 mg, yield 37%, R_f = 0.7 (PE/EA = 5:1, *v/v*), $[\alpha]_D^{25}$ = +37.5 (c 0.48, dichloromethane). ^{1}H NMR (400 MHz, DMSO-d_6) *δ* 14.03 (s, 1H), 8.48 (s, 1H), 7.37 (d, *J* = 7.1 Hz, 2H), 7.28 (d, *J* = 2.3 Hz, 1H), 7.24 – 7.19 (m, 4H), 7.18 – 7.13 (m, 3H), 7.13 – 7.09 (m, 3H), 3.96 (dd, *J* = 12.5, 6.8 Hz, 1H), 3.88 (dd, *J* = 12.4, 5.5 Hz, 1H), 3.07 (t, *J* = 6.1 Hz, 1H), 2.43 (dd, *J* = 6.3, 3.2 Hz, 1H), 2.03 (d, *J* = 6.6 Hz, 1H), 1.91 (d, *J* = 3.2 Hz, 1H), 1.35 (s, 9H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) *δ* 168.3, 158.4, 142.0, 140.8, 139.8, 136.1, 128.5, 127.9, 127.6, 127.0, 126.7, 126.6, 126.4, 118.2, 74.1, 65.6, 39.4, 38.9, 35.0, 34.3, 31.8, 29.7. IR (KBr) *ν* 3063, 3030, 2956, 2869, 1632, 1604, 1464, 1361, 1275, 1204, 1026, 750, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{31}H_{39}N_2O^+$ $[M+H]^+$: 455.3057, found 455.3062.

2,4-Diiodo-6-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3ma)
Yellow crystals, 133 mg, yield 75%, m.p. 64–66 °C, R_f = 0.4 (PE/EA = 5:1, *v/v*), $[\alpha]_D^{25}$ = +41.5 (c 1.06, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 14.84 (s, 1H), 8.05 (d, *J* = 2.1 Hz, 1H), 8.02 (s, 1H), 7.44 (d, *J* = 2.1 Hz, 1H), 7.35 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.31 – 7.25 (m, 3H), 7.25 – 7.18 (m, 3H), 7.17 – 7.12 (m, 2H), 4.03 (dd, *J* = 12.2, 7.2 Hz, 1H), 3.97 (dd, *J* = 12.3, 5.0 Hz, 1H), 3.04 (dd, *J* = 6.9, 5.5 Hz, 1H), 2.42 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.08 (d, *J* = 3.5 Hz, 1H), 1.96 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 164.3, 162.4, 149.0, 140.3, 139.9, 139.56, 128.6, 128.2, 127.8, 127.4, 126.9, 126.3, 119.4, 89.0, 78.3, 74.5, 65.1, 39.3, 38.9. IR (KBr) *ν* 3060, 3029, 2956, 2924, 2853, 1631, 1438, 1275, 1157, 1026, 867, 749, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}I_2N_2O^+$ $[M+H]^+$: 594.9738, found 594.9742.

2,4-Dibromo-6-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3na)
Yellow oil, 116 mg, yield 78%, R_f = 0.3 (PE/EA = 5:1, *v/v*), $[\alpha]_D^{25}$ = +14.4 (c 0.39, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 14.61 (s, 1H), 8.13 (s, 1H), 7.70 (d, *J* = 2.3 Hz, 1H), 7.36 (dd, *J* = 7.9, 1.3 Hz, 2H), 7.31 – 7.26 (m, 3H), 7.25 – 7.18 (m, 4H), 7.17 – 7.12 (m, 2H), 4.05 (dd, *J* = 12.2, 7.1 Hz, 1H), 3.98 (dd, *J* = 12.2, 4.6 Hz, 1H), 3.05 (dd, *J* = 6.8, 5.6 Hz, 1H), 2.42 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.09 (d, *J* = 3.5 Hz, 1H), 1.97 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 164.6, 159.1, 140.3, 139.6, 137.9, 132.8, 128.6, 128.2, 127.8, 127.5, 126.9, 126.3, 119.6, 112.8, 109.1, 74.5, 65.5, 39.3, 39.0. IR (KBr) *ν* 3062, 3030, 2961, 2925, 2853, 1634, 1495, 1447, 1377, 1261, 1207, 1024, 866, 800, 741, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}Br_2N_2O^+$ $[M+H]^+$: 500.9995, found 500.9998.

2-Bromo-4-nitro-6-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)phenol (3oa)
Yellow crystals, 105 mg, yield 75%, m.p. 193–196 °C, R_f = 0.5 (PE/EA = 1:1, *v/v*), $[\alpha]_D^{25}$ = -95.0 (c 0.98, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 15.01 (s, 1H), 8.54 (d, *J* = 2.8 Hz, 1H), 8.09 (d, *J* = 2.8 Hz, 1H), 7.95 (s, 1H), 7.33 – 7.29 (m, 3H), 7.29 – 7.27 (m, 2H), 7.25 – 7.21 (m, 1H), 7.18 (d, *J* = 1.6 Hz, 1H), 7.16 (s, 1H), 4.06 (dd, *J* = 12.8, 4.8 Hz, 1H), 3.99 (dd, *J* = 12.8, 6.1 Hz, 1H), 2.49 (dd, *J* = 6.6, 3.5 Hz, 1H), 2.15 (d, *J* = 3.5 Hz, 1H), 1.97 (d, *J* = 6.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 172.7, 166.3, 138.9, 138.4, 135.7, 132.2, 130.0, 128.9, 128.4, 127.4, 127.2, 126.2, 122.8, 117.7, 112.6, 73.3, 59.8, 39.4, 39.3. IR (KBr) *ν* 3061, 3031, 2956, 2924, 2853, 1649, 1599, 1543, 1494, 1452, 1317, 1218, 1093, 1028, 903, 746, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{21}BrN_3O_3^+$ $[M+H]^+$: 466.0761, found 466.0760.

2-((*E*)-(((*R*)-2-((*S*)-2-Benzylaziridin-1-yl)-3-phenylpropyl)imino)methyl)phenol (3ab)
Yellow oil, 77 mg, yield 67%, R_f = 0.3 (PE/EA = 1:1, *v/v*), $[\alpha]_D^{25}$ = -115.6 (c 1.35, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 13.50 (s, 1H), 8.10 (s, 1H), 7.39 – 7.31 (m, 1H), 7.30 – 7.23 (m, 3H), 7.23 – 7.15 (m, 4H), 7.15 – 7.11 (m, 2H), 7.03 (d, *J* = 6.3 Hz, 3H), 6.87 (td, *J* = 7.5, 0.9 Hz, 1H), 3.80 – 3.59 (m, 1H), 3.17 – 3.01 (m, 2H), 2.88 (dd, *J* = 13.5, 8.6 Hz, 1H), 2.72 (dd, *J* = 13.9, 4.7 Hz, 1H), 2.31 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.15 (dd, *J* = 12.1, 8.3 Hz, 1H), 1.69 (d, *J* = 3.5 Hz, 1H), 1.64 (dt, *J* = 8.1, 5.7 Hz, 1H), 1.37 (d, *J* = 6.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 164.8, 161.2, 139.0, 138.1, 132.3, 131.4, 129.5, 128.7, 128.4, 128.3, 126.4, 126.2, 118.7, 118.7, 117.0, 72.5, 65.8, 42.1, 41.0, 39.5, 33.3. IR (KBr) *ν* 3061, 3027, 2924, 2854, 1727, 1631, 1581, 1496, 1455, 1279, 1208, 1151, 1080, 804, 754, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{25}H_{27}N_2O^+$ $[M+H]^+$: 371.2118, found 371.2125. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 10:90, *v/v*, 1.0 mL/min, 260 nm), t_R = 7.36 min, ee > 99%.

2-((*E*)-(((*R*)-2-((*S*)-2-Benzylaziridin-1-yl)-3-phenylpropyl)imino)methyl)-4-methoxyphenol (3cb)
Yellow oil, 86 mg, yield 72%, R_f = 0.5 (PE/EA = 1:1, *v/v*), $[\alpha]_D^{25}$ = -117.1 (c 0.68, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 12.99 (s, 1H), 8.06 (s, 1H), 7.30 – 7.18 (m, 6H), 7.13 (d, *J* = 7.2 Hz, 2H), 7.04 (d, *J* = 6.9 Hz, 2H), 7.00 – 6.93 (m, 2H), 6.68 (d, *J* = 1.8 Hz, 1H), 3.77 (s, 3H), 3.72 – 3.63 (m, 1H), 3.08 (d, *J* = 4.2 Hz, 1H), 3.05 (d, *J* = 4.5 Hz, 1H), 2.87 (dd, *J* = 13.5, 8.6 Hz, 1H), 2.72 (dd, *J* = 13.9, 4.6 Hz, 1H), 2.30 (dd, *J* = 13.9, 7.5 Hz, 1H), 2.14 (dd, *J* = 12.1, 8.4 Hz, 1H), 1.69 (d, *J* = 3.5 Hz, 1H), 1.68 – 1.62 (m, 1H), 1.37 (d, *J* = 6.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 164.6, 155.3, 152.0, 139.0, 138.1, 129.6, 128.8, 128.4, 128.4, 126.4, 126.2, 119.3, 118.4, 117.7, 115.0, 72.6, 65.82, 55.9, 42.2, 41.0, 39.5, 33.3. IR (KBr) *ν* 3028, 2987, 2969, 2921, 2856, 1664, 1633, 1590, 1494, 1450, 1386, 1272, 1074, 1037, 759, 746, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd

for $C_{26}H_{29}N_2O_2^+$ [M+H]$^+$: 401.2224, found 401.2228. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 10:90, *v/v*, 1.0 mL/min, 254 nm), t_R = 8.49 min, ee > 99%.

2-((*E*)-(((*R*)-2-((*S*)-2-Benzylaziridin-1-yl)-3-phenylpropyl)imino)methyl)-4-nitrophenol (3fb)
Yellow oil, 118 mg, yield 95%, R_f = 0.2 (PE/EA = 1:1, *v/v*), $[\alpha]^{25}_D$ = -137.6 (c 0.98, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.84 (s, 1H), 8.23 (dd, *J* = 9.3, 2.8 Hz, 1H), 8.08 (d, *J* = 2.8 Hz, 1H), 7.93 (s, 1H), 7.33 – 7.27 (m, 3H), 7.27 – 7.19 (m, 3H), 7.16 – 7.08 (m, 4H), 7.03 (d, *J* = 9.3 Hz, 1H), 3.72 (tt, *J* = 8.6, 4.4 Hz, 1H), 3.14 (dd, *J* = 13.6, 4.6 Hz, 1H), 2.97 (dd, *J* = 12.3, 4.2 Hz, 1H), 2.88 (dd, *J* = 13.6, 9.1 Hz, 1H), 2.64 (dd, *J* = 14.1, 5.9 Hz, 1H), 2.55 (dd, *J* = 14.1, 6.3 Hz, 1H), 2.36 (dd, *J* = 12.3, 7.9 Hz, 1H), 1.76 (d, *J* = 3.4 Hz, 1H), 1.74 – 1.68 (m, 1H), 1.43 (d, *J* = 6.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 163.8, 139.0, 138.8, 137.2, 129.4, 128.7, 128.6, 128.4, 128.3, 128.2, 126.8, 126.4, 118.9, 116.6, 70.9, 65.2, 41.7, 40.7, 39.5, 33.6. IR (KBr) *v* 3061, 3028, 2958, 2925, 2853, 1725, 1634, 1531, 1487, 1454, 1338, 1093, 835, 742, 701 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{25}H_{26}N_3O_3^+$ [M+H]$^+$: 416.1969, found 416.1972. HPLC analysis: chiralpak AD-H (*i*-PrOH/hexane = 10:90, *v/v*, 1.0 mL/min, 254 nm), t_R = 12.81 min, ee > 99%.

2-((*E*)-(((*R*)-2-((*S*)-2-Benzylaziridin-1-yl)-3-phenylpropyl)imino)methyl)-4,6-di-*tert*-butylphenol(3lb)
Yellow oil, 88 mg, yield 60%, R_f = 0.2 (PE/EA = 5:1, *v/v*), $[\alpha]^{25}_D$ = -83.2 (c 0.6, dichloromethane). ^{1}H NMR (400 MHz, Acetone−d_6) δ 14.04 (s, 1H), 8.36 (s, 1H), 7.46 (s, 1H), 7.29 – 7.12 (m, 9H), 7.02 (d, *J* = 7.5 Hz, 2H), 3.75 – 3.67 (m, 1H), 3.12 (dd, *J* = 13.5, 5.3 Hz, 1H), 2.93 (dd, *J* = 13.5, 8.2 Hz, 1H), 2.86 (dd, *J* = 11.9, 4.2 Hz, 1H), 2.67 (dd, *J* = 14.1, 4.3 Hz, 1H), 2.32 (dd, *J* = 13.9, 6.9 Hz, 1H), 2.22 (dd, *J* = 12.0, 8.1 Hz, 1H), 1.59 (t, *J* = 4.3 Hz, 2H), 1.48 (s, 9H), 1.30 (s, 9H), 0.95 – 0.81 (m, 1H). ^{13}C NMR (101 MHz, Acetone−d_6) δ 167.2, 159.1, 140.9, 140.5, 139.7, 137.0, 130.4, 129.6, 129.1, 129.0, 127.4, 127.1, 127.0, 126.8, 119.1, 72.8, 66.5, 42.3, 41.5, 40.3, 35.7, 34.7, 33.6, 31.9, 31.8. IR (KBr) *v* 3007, 2966, 2921, 2882, 2856, 1731, 1632, 1472, 1441, 1384, 1357, 1279, 1255, 1174, 1078, 880, 819, 751, 697 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{33}H_{43}N_2O^+$ [M+H]$^+$: 483.3370, found 483.3379. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 10:90, *v/v*, 1.0 mL/min, 260 nm), t_R = 4.13 min, ee > 99%.

2-((*E*)-(((*R*)-2-((*S*)-2-Benzylaziridin-1-yl)-3-phenylpropyl)imino)methyl)-4,6-diiodophenol (3mb)
Yellow oil, 163 mg, yield 87%, R_f = 0.2 (PE/EA = 1:1, *v/v*), $[\alpha]^{25}_D$ = -113.9 (c 1.22, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.00 (s, 1H), 8.06 (d, *J* = 2.0 Hz, 1H), 7.68 (s, 1H), 7.31 (d, *J* = 2.0 Hz, 1H), 7.29 – 7.25 (m, 3H), 7.25 – 7.16 (m, 3H), 7.11 – 7.03 (m, 4H), 3.68 (tt, *J* = 8.5, 4.2 Hz, 1H), 3.06 (dd, *J* = 13.8, 4.7 Hz, 1H), 3.01 (dd, *J* = 12.4, 4.2 Hz, 1H), 2.80 (dd, *J* = 13.6, 9.1 Hz, 1H), 2.59 (dd, *J* = 14.0, 5.0 Hz, 1H), 2.39 (dd, *J* = 14.0, 6.6 Hz, 1H), 2.20 (dd, *J* = 12.2, 8.4 Hz, 1H), 1.70 (d, *J* = 3.1 Hz, 1H), 1.69 – 1.63 (m, 1H), 1.37 (d, *J* = 6.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 161.8, 148.7, 139.9, 138.8, 137.4, 129.4, 128.8, 128.6, 128.5, 126.7, 126.3, 119.4, 88.4, 78.7, 71.3, 65.5, 42.1, 40.8, 39.7, 33.5. IR (KBr) *v* 3059, 3026, 2955, 2924, 2852, 1626, 1495, 1438, 1374, 1276, 1079, 868, 749, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{25}H_{25}I_2N_2O^+$ [M+H]$^+$: 623.0051, found 623.0054. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 5:95, *v/v*, 0.8 mL/min, 254 nm), t_R = 20.49 min, ee > 99%.

2-((*E*)-(((*R*)-2-((*S*)-2-Benzylaziridin-1-yl)-3-phenylpropyl)imino)methyl)-4,6-dibromophenol (3nb)
Yellow oil, 118 mg, yield 74%, R_f = 0.2 (PE/EA = 1:1, *v/v*), $[\alpha]^{25}_D$ = -125.3 (c 1.17, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.69 (s, 1H), 7.65 (s, 1H), 7.60 (d, *J* = 2.3 Hz, 1H), 7.18 – 7.13 (m, 3H), 7.13 – 7.04 (m, 3H), 7.03 (d, *J* = 2.3 Hz, 1H), 6.99 – 6.93 (m, 4H), 3.56 (tt, *J* = 8.5, 4.2 Hz, 1H), 2.96 (dd, *J* = 13.6, 4.5 Hz, 1H), 2.90 (dd, *J* = 12.2, 4.0 Hz, 1H), 2.69 (dd, *J* = 13.6, 9.1 Hz, 1H), 2.48 (dd, *J* = 14.0, 5.1 Hz, 1H), 2.29 (dd, *J* = 14.0, 6.6 Hz, 1H), 2.10 (dd, *J* = 12.2, 8.4 Hz, 1H), 1.59 (d, *J* = 3.3 Hz, 1H), 1.58 – 1.53 (m, 1H), 1.26 (d, *J* = 6.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 158.6, 138.9, 137.7, 137.4, 132.8, 129.4, 128.8, 128.6, 128.4, 126.7, 126.3, 119.6, 112.6, 109.2, 71.5, 65.5, 42.0, 40.80, 39.7, 33.5. IR (KBr) *v* 3062, 3028, 2959, 2924, 2853, 1733, 1632, 1496, 1447, 1377, 1263, 1166, 1089, 867. 803, 742, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{25}H_{25}Br_2N_2O^+$ [M+H]$^+$: 529.0308, found 529.0309.

2-((*E*)-(((*R*)-2-((*S*)-2-Isopropylaziridin-1-yl)-3-methylbutyl)imino)methyl)phenol (3ac)
Yellow oil, 53 mg, yield 64%, R_f = 0.7 (PE/EA = 1:1, *v/v*), $[\alpha]^{25}_D$ = +81.9 (c 0.36, dichloromethane). ^{1}H NMR (400 MHz, Acetone−d_6) δ 13.57 (s, 1H), 8.52 (s, 1H), 7.40 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.34 – 7.28 (m, 1H), 6.94 – 6.85 (m, 2H), 3.24 (dt, *J* = 8.0, 4.6 Hz, 1H), 2.58 (dd, *J* = 12.0, 4.7 Hz, 1H), 2.36 (dd, *J* = 12.0, 7.8 Hz, 1H), 2.13 – 2.03 (m, 1H), 1.48 (d, *J* = 1.0 Hz, 1H), 1.23 – 1.15 (m, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.79 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, Acetone−d_6) δ 165.4, 161.4, 131.9, 131.5, 119.1, 118.3, 116.5, 75.3, 64.3, 46.3, 31.2, 30.7, 30.7, 19.8, 19.4, 18.5, 17.0. IR (KBr) *v* 3060, 2987, 2960, 2927, 1747, 1660, 1631, 1581, 1494, 1461, 1392, 1278, 1076, 1049, 869, 757, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{17}H_{27}N_2O^+$ [M+H]$^+$: 275.2118, found 275.2122. HPLC analysis: chiralpak AD-H (*i*-PrOH/hexane = 10:90, *v/v*, 0.8 mL/min, 254 nm), t_R = 4.39 min, ee > 99%.

2-((*E*)-(((*R*)-2-((*S*)-2-Isopropylaziridin-1-yl)-3-methylbutyl)imino)methyl)-4-nitrophenol (3fc)
Yellow oil, 82 mg, yield 86%, R_f = 0.3 (PE/EA = 1:1, *v/v*), $[\alpha]^{25}_D$ = +57.6 (c 0.41, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.06 (s, 1H), 8.38 (s, 1H), 8.25 (d, *J* = 2.8 Hz, 1H), 8.18 (dd, *J* = 9.3, 2.8 Hz, 1H), 6.93 (d, *J* = 9.3 Hz, 1H), 3.59 – 3.15 (m, 1H), 2.62 (dd, *J* = 12.4, 4.0 Hz, 1H), 2.41 (dd, *J* = 12.4, 8.4 Hz, 1H), 2.05 (qd, *J* = 11.7, 6.8 Hz, 1H), 1.57 (d, *J* = 2.8 Hz, 1H), 1.24 (s, 1H), 1.22 – 1.17 (m, 2H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.3 Hz, 3H), 0.79 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 164.2, 138.2, 128.8, 128.5, 119.7, 116.2, 73.8, 63.7, 47.2, 32.1, 31.0 29.7, 20.4, 19.7 19.0, 17.6. IR (KBr) *v* 3063, 3035, 2957, 2925, 2854, 1643, 1612, 1542, 1324, 1236, 1092, 836, 750 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{17}H_{26}N_3O_3^+$ [M+H]$^+$: 320.1969, found 320.1977. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 10:90, *v/v*, 1.0 mL/min, 254 nm), t_R = 5.54 min, ee > 99%.

2,4-Diiodo-6-((*E*)-(((*R*)-2-((*S*)-2-isopropylaziridin-1-yl)-3-methylbutyl)imino)methyl)phenol (3mc)
Yellow oil, 113 mg, yield 71%, R_f = 0.2 (PE/EA = 5:1, *v/v*), $[\alpha]^{25}_D$ = +93.4 (c 0.74, dichloromethane). ^{1}H NMR (400 MHz, Acetone−d_6) δ 15.25 (s, 1H), 8.46 (s, 1H), 8.07 (d, *J* = 2.0 Hz, 1H), 7.75 (d, *J* = 2.0 Hz, 1H), 3.45 – 3.37 (m, 1H), 2.56 (dd, *J* = 12.2, 8.0 Hz, 1H), 2.49 (dd, *J* = 12.3, 4.6 Hz, 1H), 2.15 – 2.08 (m, 1H), 1.51 (d, *J* = 2.2 Hz, 1H), 1.24 – 1.16 (m, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.79 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, Acetone−d_6) δ 165.1, 164.5, 149.3, 141.3, 120.2, 90.2, 77.5, 73.9, 64.3, 47.1, 32.3, 31.6, 31.4, 20.6, 20.1, 19.3, 17.9. IR (KBr) *v* 3172, 2965, 2925, 2900, 1635, 1614, 1538, 1489, 1467, 1407, 1382, 1334, 1228 1074, 894, 833, 754, 696, 632 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{17}H_{25}I_2N_2O^+$ [M+H]$^+$: 527.0051, found 527.0056. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 5:95, *v/v*, 0.9 mL/min, 254 nm), t_R = 4.723 min, ee > 99%.

2,4-Dibromo-6-((*E*)-(((*R*)-2-((*S*)-2-isopropylaziridin-1-yl)-3-methylbutyl)imino)methyl)phenol (3nc)
Yellow oil, 90 mg, yield 69%, R_f = 0.3 (PE/EA = 1:1, *v/v*), $[\alpha]^{25}_D$ = +79.9 (c 0.69, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.96 (s, 1H), 8.21 (s, 1H), 7.69 (d, *J* = 2.3 Hz, 1H), 7.32 (d, *J* = 2.3 Hz, 1H), 3.51 – 3.14 (m, 1H), 2.69 (dd, *J* = 12.3, 4.0 Hz, 1H), 2.29 (dd, *J* = 12.3, 8.4 Hz, 1H), 2.07 – 1.88 (m, 1H), 1.54 (s, 1H), 1.20 – 1.13 (m, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.1 Hz, 3H), 0.78 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz,

$CDCl_3$) δ 163.3, 160.0, 137.9, 132.7, 119.3, 113.2, 108.5, 74.5, 64.0, 47.2, 32.0, 31.1, 31.0, 20.5, 19.8, 19.0, 17.6. IR (KBr) ν 3070, 3043, 2959, 2926, 2853, 1632, 1447, 1376, 1288, 1166, 1021, 866, 804, 746, 692 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{17}H_{25}Br_2N_2O^+$ $[M+H]^+$: 433.0308, found 433.0309. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 1:99, *v/v*, 0.9 mL/min, 254 nm), t_R = 6.07 min, ee > 99%.

2-((*E*)-1-(((*R*)-2-Phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)ethyl)phenol (3pa)
Yellow oil, 18 mg, yield 17%, R_f = 0.2 (PE/EA = 5:1, *v/v*), $[\alpha]^{25}_D$ = +112.3 (c 0.10, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.14 (s, 1H), 7.49 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.31 – 7.26 (m, 3H), 7.25 – 7.20 (m, 3H), 7.20 – 7.15 (m, 3H), 6.94 (dd, *J* = 8.3 Hz, 1.0, 1H), 6.80 – 6.74 (m, 1H), 4.08 (dd, *J* = 14.1, 6.7 Hz, 1H), 3.92 (dd, *J* = 14.1, 6.0 Hz, 1H), 3.09 (t, *J* = 6.3 Hz, 1H), 2.45 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.27 (s, 3H), 2.14 (d, *J* = 3.5 Hz, 1H), 2.08 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 163.7, 141.3, 139.9, 132.4, 128.4, 128.1, 128.1, 127.6, 127.5, 126.7, 126.3, 119.4, 118.6, 117.1, 75.2, 57.0, 39.4, 39.1, 14.5. IR (KBr) ν 3061, 3030, 2955, 2922, 2851, 1614, 1496, 1455, 1378, 1260, 1023, 801, 752, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{24}H_{25}N_2O^+$ $[M+H]^+$: 357.1961, found 357.1968.

2-((*E*)-(((1*R*,2*S*)-2-((1*R*,6*S*)-7-Azabicyclo[4.1.0]heptan-7-yl)cyclohexyl)imino)methyl)-4-nitrophenol (3fd)
Yellow crystals, 72 mg, yield 70%, m.p. 147–149 °C, R_f = 0.3 (PE/EA = 1:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.07 (s, 1H), 8.44 (s, 1H), 8.23 (d, *J* = 2.8 Hz, 1H), 8.17 (dd, *J* = 9.3, 2.8 Hz, 1H), 6.92 (d, *J* = 9.3 Hz, 1H), 3.49 – 3.28 (m, 1H), 1.98 – 1.89 (m, 1H), 1.88 – 1.75 (m, 3H), 1.74 – 1.65 (m, 2H), 1.63 – 1.47 (m, 3H), 1.46 – 1.32 (m, 4H), 1.26 – 0.93 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 162.9, 138.3, 128.4, 119.6, 116.3, 73.2, 72.6, 40.0, 35.0, 33.0, 30.7, 24.6, 24.5, 24.4, 20.4, 20.4. IR (KBr) ν 3068, 2932, 2850, 1634, 1450, 1291, 1163, 1085, 850, 802, 749, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{19}H_{26}N_3O_3^+$ $[M+H]^+$: 344.1969, found 344.1973.

2-((*E*)-(((1*R*,2*S*)-2-((1*R*,6*S*)-7-Azabicyclo[4.1.0]heptan-7-yl)cyclohexyl)imino)methyl)-4,6-dibromophenol (3nd)
Yellow solid, 87 mg, yield 64%, m.p. 139–142 °C, R_f = 0.3 (PE/EA = 1:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.05 (s, 1H), 8.30 (s, 1H), 7.68 (d, *J* = 2.4 Hz, 1H), 7.31 (d, *J* = 2.4 Hz, 1H), 3.33 (ddd, *J* = 12.0, 8.3, 4.0 Hz, 1H), 1.92 (dd, *J* = 6.4, 2.6 Hz, 1H), 1.83 – 1.73 (m, 3H), 1.71 – 1.64 (m, 2H), 1.62 – 1.46 (m, 3H), 1.44 – 1.33 (m, 4H), 1.28 – 0.95 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 160.1, 137.8, 132.5, 119.4, 113.2, 108.5, 73.6, 72.8, 39.9, 35.0, 33.2, 30.7, 24.6, 24.4, 24.4, 20.5, 20.4. IR (KBr) ν 3071, 2930, 2857, 1631, 1447, 1377, 1288, 1167, 1070, 866, 815, 741, 701, 686, cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{19}H_{25}Br_2N_2O^+$ $[M+H]^+$: 457.0308, found 457.0313.

(*E*)-2-(((2-(2,2-Dimethylaziridin-1-yl)-2-methylpropyl)imino)methyl)-4-nitrophenol (3fe)
Yellow solid, 38 mg, yield 52%, m.p. 171–122 °C, R_f = 0.1 (PE/EA = 1:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.30 (s, 1H), 8.35 (s, 1H), 8.24 (d, *J* = 2.9 Hz, 1H), 8.11 (dd, *J* = 9.6, 2.9 Hz, 1H), 6.76 (d, *J* = 9.6 Hz, 1H), 2.75 (d, *J* = 12.6 Hz, 1H), 2.29 (d, *J* = 12.6 Hz, 1H), 1.77 (s, 1H), 1.48 (s, 3H), 1.47 (s, 3H), 1.16 (s, 3H), 1.11 (s, 3H), 1.11 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.2, 162.1, 135.8, 131.2, 129.5, 122.6, 113.8, 62.6, 59.9, 42.6, 35.6, 26.5, 25.6, 25.3, 17.7. IR (KBr) ν 3067, 3040, 2959, 2926, 2870, 2854, 1643, 1613, 1540, 1324, 1293, 1237, 1092, 942, 837, 731, 667, cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{15}H_{22}N_3O_3^+$ $[M+H]^+$: 292.1656, found 292.1664.

***N*-Methyl-2-((*E*)-(((*R*)-2-phenyl-2-((*S*)-2-phenylaziridin-1-yl)ethyl)imino)methyl)aniline (8a)**
Yellow oil, 22 mg, yield 30%, R_f = 0.7 (PE/EA = 5:1, *v/v*), $[\alpha]^{25}_D$ = +72.4 (c 0.32, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 4.1 Hz, 1H), 8.36 (s, 1H), 7.51 – 7.40 (m, 2H), 7.32 – 7.27 (m, 3H), 7.26 – 7.22 (m, 3H), 7.22 – 7.16 (m, 4H), 6.70 – 6.59 (m, 2H), 4.02 (dd, *J* = 12.3, 6.9 Hz, 1H), 3.95 (ddd, *J* = 12.1, 5.7, 1.0 Hz, 1H), 3.00 – 2.93 (m, 1H), 2.90 (d, *J* = 5.1 Hz, 3H), 2.41 (dd, *J* = 6.5, 3.5 Hz, 1H), 2.11 (d, *J* = 3.5 Hz, 1H), 2.03 (d, *J* = 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 150.3, 142.0, 140.1, 133.9, 131.5, 128.2, 128.1, 127.6, 127.2, 126.7, 126.4, 117.1, 114.2, 109.5, 75.9, 68.7, 39.2, 39.0, 29.2. IR (KBr) ν 3265, 3064, 3030, 2956, 2925, 2852, 1657, 1630, 1606, 1581, 1495, 1462, 1333, 1204 1170, 1026, 870, 747, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{24}H_{26}N_3^+$ $[M+H]^+$: 356.2121, found 356.2124. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 10:90, *v/v*, 1.0 mL/min, 230 nm), t_R = 5.97 min, ee > 99%.

2-((*E*)-(((*R*)-2-((*S*)-2-Benzylaziridin-1-yl)-3-phenylpropyl)imino)methyl)-*N*-methylaniline (8b)
Yellow oil, 37 mg, yield 32%, R_f = 0.3 (PE/EA = 5:1, *v/v*), $[\alpha]^{25}_D$ = -80.8 (c 0.25, dichloromethane). ^{1}H NMR (400 MHz, Acetone−d_6) δ 9.21 (d, *J* = 3.9 Hz, 1H), 8.24 (s, 1H), 7.33 – 7.15 (m, 10H), 7.11 (d, *J* = 7.4 Hz, 2H), 6.72 (d, *J* = 8.3 Hz, 1H), 6.62 (t, *J* = 7.3 Hz, 1H), 3.64 – 3.52 (m, 1H), 3.10 (dd, *J* = 13.3, 5.0 Hz, 1H), 2.94 – 2.90 (m, 4H), 2.88 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.72 (dd, *J* = 13.8, 3.8 Hz, 1H), 2.35 (dd, *J* = 13.8, 6.4 Hz, 1H), 2.12 (dd, *J* = 11.6, 7.8 Hz, 1H), 1.61 (s, 2H), 1.28 (d, *J* = 5.7 Hz, 1H). ^{13}C NMR (101 MHz, Acetone−d_6) δ 164.9, 151.4, 140.8, 140.2, 134.7, 132.3, 130.7, 129.7, 129.1, 129.0, 126.9, 126.9, 118.2, 115.1, 110.3, 74.3, 66.9, 42.5, 42.0, 40.3, 33.7, 29.5. IR (KBr) ν 3361, 3046, 2969, 2929, 2894, 1660, 1627, 1442, 1380, 1278, 1085, 1047, 879, 744, 701, 657 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{26}H_{30}N_3^+$ $[M+H]^+$: 384.2434, found 384.2442. HPLC analysis: Lux 5μ cellulose-1 (*i*-PrOH/hexane = 15:85, *v/v*, 0.7 mL/min, 230 nm), t_R = 7.62 min, ee > 99%.

General procedure for the enantioselective aldol reaction of aromatic aldehydes 9 and acetone

Ligand (0.055 mmol) and $Zn(OTf)_2$ (0.050 mmol, 18.2 mg) were stirred in 2 mL of acetone/H_2O (9:1, *v/v*) for 20 min at r.t., then, aromatic aldehyde **9** (0.50 mmol) was added and the resulting mixture was stirred for appropriate time at r.t.. The reaction mixture was quenched with a saturated aqueous ammonium chloride solution and then extracted with ethyl acetate (3×10 mL). The organic layer was dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (5:1, *v/v*) as eluent to afford the pure aldol product. The enantiomeric excess was determined by chiral HPLC with Daicel Chiralpak AS-H/AD-H with *i*-PrOH/hexane as eluent.

(*R*)-4-Hydroxy-4-(4-nitrophenyl)butan-2-one (10a)
Using ligand **3mc**: white solid, yield 90%, m.p. 59–60 °C, Lit.[19f] m.p. 58–60 °C, R_f = 0.2 (PE/EA = 5:1, *v/v*), ee 94%, $[\alpha]^{25}_D$ = +37.0 (c 0.54, $CHCl_3$), Lit.[19a] $[\alpha]^{25}_D$ = +35.2 (c 0.2, $CHCl_3$). HPLC analysis: chiralpak AS-H (*i*-PrOH/hexane = 20:80, *v/v*, 1.0 mL/min, 260 nm) major t_R = 13.81 min and minor t_R = 18.66 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 5.27 (t, *J* = 5.4 Hz, 1H), 3.76 (s, 1H), 2.87 (d, *J* = 6.2 Hz, 2H), 2.23 (s 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.5, 150.1, 147.3, 126.4, 123.7, 68.9, 51.5, 30.7.

(*R*)-4-Hydroxy-4-(3-nitrophenyl)butan-2-one (10b)
Using ligand **3mc**: yellow oil, yield 86%, R_f = 0.5 (PE/EA = 2:1, *v/v*), ee 78%, $[\alpha]^{25}_D$ = +65.8 (c 0.6, $CHCl_3$), Lit.[19d] $[\alpha]^{27}_D$ = +63.1 (c 0.5, $CHCl_3$). HPLC analysis: chiralpak AD-H (*i*-PrOH/hexane = 10:90, *v/v*, 1.0 mL/min, 260 nm) major t_R = 15.43 min and minor t_R = 16.22 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.15 – 8.10 (m, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 5.30 – 5.22 (m, 1H), 3.67 (d, *J* = 3.1 Hz, 1H), 2.97 – 2.82 (m, 2H), 2.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.6, 148.4, 144.9, 131.8, 129.5, 122.6, 120.7, 68.8, 51.5, 30.7.

(*R*)-4-Hydroxy-4-(2-nitrophenyl)butan-2-one (10c)
Using ligand **3mc**: yellow oil, yield 95%, R_f = 0.5 (PE/EA = 2:1, *v*/*v*), ee 81%, $[\alpha]^{25}_{D}$ = -142.6 (c 0.78, $CHCl_3$), Lit.[19d] $[\alpha]^{27}_{D}$ = -157.6 (c 0.3, $CHCl_3$). HPLC analysis: chiralpak AD-H (*i*-PrOH/hexane = 5:95, *v*/*v*, 1.0 mL/min, 260 nm) major t_R = 23.21 min and minor t_R = 24.32 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.1 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 5.68 (d, *J* = 9.3 Hz, 1H), 3.76 (s, 1H), 3.13 (dd, *J* = 17.8, 1.8 Hz, 1H), 2.73 (dd, *J* = 17.8, 9.4 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 147.2, 138.4, 133.8, 128.3, 128.2, 124.5, 65.7, 51.1, 30.5.

(*R*)-4-(1-Hydroxy-3-oxobutyl)benzonitrile (10d)
Using ligand **3mc**: yellow oil, yield 85%, R_f = 0.4 (PE/EA = 2:1, *v*/*v*), ee 75%, $[\alpha]^{25}_{D}$ = +81.1 (c 0.62, $CHCl_3$), Lit.[19g] $[\alpha]^{22}_{D}$ = +74.3 (c 0.48, $CHCl_3$). HPLC analysis: chiralpak AS-H (*i*-PrOH/hexane = 30:70, *v*/*v*, 1.0 mL/min, 230 nm) major t_R = 10.52 min and minor t_R = 17.68 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 5.22 (d, *J* = 6.3 Hz, 1H), 3.59 (d, *J* = 2.9 Hz, 1H), 2.96 – 2.73 (m, 2H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.6, 148.0, 132.4, 126.3, 118.7, 111.4, 69.1, 51.5, 30.7.

(*R*)-4-(4-Chlorophenyl)-4-hydroxybutan-2-one (10e)
Using ligand **3mc**: white solid, yield 80%, m.p. 52–54 °C, Lit.[19d] m.p. 50 °C, R_f = 0.5 (PE/EA = 2:1, *v*/*v*), ee 77%, $[\alpha]^{25}_{D}$ = +62.0 (c 0.48, $CHCl_3$), Lit.[19g] $[\alpha]^{22}_{D}$ = 70.5 (c 0.5, $CHCl_3$). HPLC analysis: chiralpak AS-H (*i*-PrOH/hexane = 15:85, *v*/*v*, 1.0 mL/min, 220 nm) major t_R = 8.91 min and minor t_R = 10.28 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 4H), 5.13 (dd, *J* = 8.2, 4.1 Hz, 1H), 3.37 (s, 1H), 2.91 – 2.75 (m, 2H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.9, 141.2, 133.3, 128.7, 127.0, 69.2, 51.8, 30.7.

(*R*)-4-(4-Bromophenyl)-4-hydroxybutan-2-one (10f)
Using ligand **3mc**: white solid, yield 82%, m.p. 57–59 °C, Lit.[19d] m.p. 58–60 °C, R_f = 0.5 (PE/EA = 2:1, *v*/*v*), ee 83%, $[\alpha]^{25}_{D}$ = +42.2 (c 0.36, $CHCl_3$), Lit.[19g] $[\alpha]^{20}_{D}$ = +54.5 (c 0.51, $CHCl_3$). HPLC analysis: chiralpak AS-H (*i*-PrOH/hexane = 20:80, *v*/*v*, 1.0 mL/min, 220 nm) major t_R = 7.54 min and minor t_R = 8.81 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 5.10 (d, *J* = 4.5 Hz, 1H), 3.40 (s, 1H), 2.88 – 2.73 (m, 2H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 141.7, 131.6, 127.3, 121.4, 69.2, 51.72, 30.7.

(*R*)-4-Hydroxy-4-(3-methoxyphenyl)butan-2-one (10g)
Using ligand **3mc**: yellow oil, yield 69%, R_f = 0.5 (PE/EA = 2:1, *v*/*v*), ee 81%, $[\alpha]^{25}_{D}$ = +54.8 (c 0.5, $CHCl_3$), Lit.[19f] $[\alpha]^{25}_{D}$ = +48.5 (c 0.7, $CHCl_3$). HPLC analysis: chiralpak AS-H (*i*-PrOH/hexane = 15:85, *v*/*v*, 1.0 mL/min, 210 nm) major t_R = 11.48 min and minor t_R = 13.07 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 9.0, 6.7 Hz, 1H), 6.92 (t, *J* = 5.6 Hz, 2H), 6.84 – 6.77 (m, 1H), 5.13 (dt, *J* = 8.8 Hz, 3.1, 1H), 3.81 (s, 3H), 3.29 (d, *J* = 3.1 Hz, 1H), 2.88 (dd, *J* = 17.5, 9.0 Hz, 1H), 2.80 (dd, *J* = 17.5, 3.4 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.0, 159.8, 144.5, 129.6, 117.9, 113.2, 111.1, 69.8, 55.3, 52.0, 30.8.

(*R*)-4-Hydroxy-4-(naphthalen-2-yl)butan-2-one (10h)
Using ligand **3mc**: yellow oil, yield 74%, R_f = 0.6 (PE/EA = 2:1, *v*/*v*), ee 81%, $[\alpha]^{25}_{D}$ = +39.8 (c 0.45, $CHCl_3$), Lit.[19h] $[\alpha]^{25}_{D}$ = +47.1 (c 0.34, $CHCl_3$). HPLC analysis: chiralpak AS-H (*i*-PrOH/hexane = 15:85, *v*/*v*, 1.0 mL/min, 210 nm) major t_R = 10.86 min and minor t_R = 11.72 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.79 (m, 4H), 7.51 – 7.43 (m, 3H), 5.30 (dt, *J* = 9.0, 3.2 Hz, 1H), 3.66 (d, *J* = 3.3 Hz, 1H), 2.94 (dd, *J* = 17.3, 9.2 Hz, 1H), 2.84 (dd, *J* = 17.3 Hz, 3.3, 1H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 140.2, 133.1, 132.8, 128.2, 127.9, 127.5, 126.1, 125.8, 124.2, 123.7, 69.8, 51.8, 30.6.

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