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Ligand and substrate π-stacking interaction controlled enantioselectivity in the asymmetric aziridination

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Abstract—Both the steric hindrance and the electronic effect are important factors for controlling the enantioselectivity in asymmetric catalysis. The substituent-dependent enantioselectivity in the asymmetric aziridination of chalcones catalyzed by 1,8-anthracene-linked bis-oxazoline (AnBOX) was rationalized to the π-stacking interaction between the ligand backbone and substrates and primarily confirmed by the use of bulky substrates and catalysts without aromatic backbones. The results provide important information for designing novel ligands and for understanding the influence of the electronic effect in asymmetric catalysis.

1. Introduction

Interactions between aromatic rings or other unsaturated systems, including π-stacking and face-to-edge complexes, are at the origin of many phenomena in both organic and biological chemistry. It is well known that the interactions play an important role in the stabilization of the stereo-structure of DNA[1] and the tertiary structure of many proteins.[2] The stability and macroscopic properties of many liquid crystal phases have been proven to originate from an aromatic π-stacking interaction.[3] Over the last two decades, it has been found that the π-stacking interactions are key factors in the chiral recognition. The arene–arene π-stacking interactions are very important in inclusion complexes, such as cyclophanes and molecular clefts.[4] Some of chromatographic chiral stationary phases were designed and prepared on the basis of the aromatic π-stacking interaction.[5] It is also well documented that π-stacking interactions play a crucial role in some asymmetric inductions.[6] Some chiral auxiliaries, such as Corey's 8-phenylmenthol[7] and Evans' oxazolidinone-based chiral auxiliaries,[8] show excellent asymmetric induction due to intramolecular aromatic π-stacking interactions between the auxiliaries and the substrates. Rappe et al. first proposed the π-stacking interaction as a factor in organometallic reactions involving aromatic substrates and ligands with aryl substituents after their theoretical investigation on the platinum-catalyzed asymmetric hydroformylation of olefins.[9] Sharpless et al. reported the first example on the influence of the ligand–substrate π-stacking interaction in the asymmetric dihydroxylation of olefins.[10] Jacobsen et al. elucidated the enantiofacial selective binding of prochiral styrenes to a chiral catalyst via simultaneous face-to-face and edge-to-face aromatic interactions in the C_2-symmetric 1,2-diimine-copper complex catalyzed aziridination and cyclopropanation. However, no influence of the electronic effect of substrates on the enantioselectivity existed in their system.[11] Recently Brandt and Andersson et al. observed that the achiral coligand–substrate aromatic π-stacking interaction plays an important role in the enantioselective Ru(arene)(amino alcohol)-catalyzed transfer hydrogenation of ketones with an obvious influence of the electronic effect of substrates on the enantioselectivity.[12] They concluded that the electrostatic effects are of importance for aromatic π-stacking interaction. These results clearly indicate that the ligand–substrate attractive aromatic π-stacking interaction can generally reduce conformational degrees of freedom and enhance chiral discrimination in the selectivity-determining transition state. To the best of our knowledge, although many examples on the aromatic π-stacking interaction on the diastereoselectivity in the *asymmetric synthesis* with aromatic chiral auxiliaries were reported,[6] only a few examples have been observed on the obvious effect of the ligand–substrate

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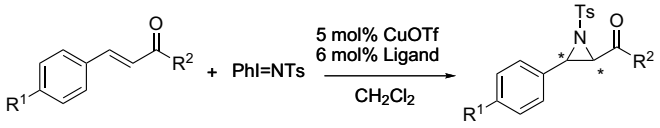
aromatic π-stacking interaction on the enantioselectivity in asymmetric catalysis.[10–12]

2. Results and discussion

We recently observed that the 1,8-anthracene-linked bis-oxazoline (AnBOX) ligand shows obvious substituent-dependent enantioselectivity in the asymmetric aziridination of chalcones (Table 1, entries 1–6).[13] Electron-rich chalcones show higher enantioselectivities than electron-deficient ones. It seemed that the electronic effect-dependent enantioselectivity was related to the Lewis basicity of the oxygen atom of the carbonyl group in chalcones. The oxygen atom of electron-rich chalcones showed a stronger Lewis basicity to facilitate a stronger coordination with the catalyst, resulting in higher enantioselectivity because the stronger coordination would preferentially allow the reaction to proceed via the asymmetric catalytic path, as observed in the asymmetric borane reduction of ketones catalyzed by chiral boroxazolidines.[14] The substrate electronic effect-dependent enantioselectivity also indicated that the coordination step is an enantioselectivity-determining step in the catalytic cycle.[13b,14] However, after conducting cyclohexane-linked bis-oxazoline (*c*HBOXes) catalyzed asymmetric aziridination of chalcones,[15] we found that *c*HBOXes did not show obvious substrate-dependent enantioselectivity. This suggests that the electronic effect-dependent enantioselectivity of AnBOX could not be simply attributed to the Lewis basicity of the carbonyl group in chalcones (Scheme 1).

To further study this phenomenon, we conducted the asymmetric aziridination of chalcones with Evans' ligand (BOX).[16] These results indicate that no obvious influence of the electronic effect of substrates on the enantioselectivity was observed when under the catalysis of *c*HBOX (Table 1, entries 8–13).[15] This caused us to assume that the AnBOX ligand shows obvious substrate electronic effect-dependent enantioselectivity possibly due to the ligand–substrate aromatic π-stacking interaction because the AnBOX ligand possesses an aromatic anthracene backbone, which locates in an appropriate position to form the π-stacking interaction with chalcones in our proposed

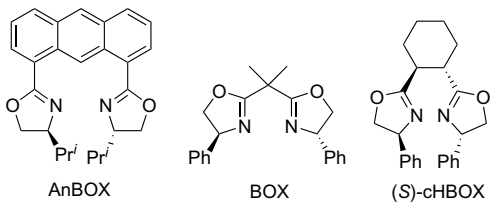
Table 1. Catalytic asymmetric aziridination of α,β-unsaturated ketones



1 2

Entry	Ligand	Product	R^1	R^2	Yield[a] (%)	ee[b] (%)	Configuration[c]
1	AnBOX	**2a**	H	4-MeC_6H_4	92	>99	(2*S*,3*R*)
2	AnBOX	**2b**	H	Ph	80	96	(2*S*,3*R*)
3	AnBOX	**2c**	H	4-FC_6H_4	72	54	(2*S*,3*R*)
4	AnBOX	**2d**	H	4-ClC_6H_4	74	58	(2*S*,3*R*)
5	AnBOX	**2e**	H	4-BrC_6H_4	64	50	(2*S*,3*R*)
6	AnBOX	**2f**	H	4-$CF_3C_6H_4$	70	44	(2*S*,3*R*)[d]
7	*S*-cBOX	*ent*-**2f**	H	4-$CF_3C_6H_4$	56	85	(2*R*,3*S*)[d]
8	BOX	*ent*-**2a**	H	4-MeC_6H_4	24	85	(2*R*,3*S*)
9	BOX	*ent*-**2b**	H	Ph	38	86	(2*R*,3*S*)
10	BOX	*ent*-**2c**	H	4-FC_6H_4	10	86	(2*R*,3*S*)
11	BOX	*ent*-**2d**	H	4-ClC_6H_4	10	81	(2*R*,3*S*)
12	BOX	*ent*-**2e**	H	4-BrC_6H_4	12	84	(2*R*,3*S*)
13	BOX	*ent*-**2f**	H	4-$CF_3C_6H_4$	4	65	(2*R*,3*S*)
14	AnBOX	**2g**	H	4-^{i}PrC_6H_4	72	66	(2*S*,3*R*)[d]
15	BOX	*ent*-**2g**	H	4-^{i}PrC_6H_4	6	76	(2*R*,3*S*)[d]
16	*S*-*c*HBOX	*ent*-**2g**	H	4-^{i}PrC_6H_4	24	85	(2*R*,3*S*)[d]
17	AnBOX	**2h**	H	4-^{t}BuC_6H_4	79	70	(2*S*,3*R*)[d]
18	BOX	*ent*-**2h**	H	4-^{t}BuC_6H_4	10	87	(2*R*,3*S*)[d]
19	*S*-*c*HBOX	*ent*-**2h**	H	4-^{t}BuC_6H_4	43	98	(2*R*,3*S*)[d]
20	AnBOX	**2i**	Me	4-^{t}BuC_6H_4	86	71	(2*S*,3*R*)[d]
21	BOX	*ent*-**2i**	Me	4-^{t}BuC_6H_4	7	81	(2*R*,3*S*)[d]
22	*S*-*c*HBOX	*ent*-**2i**	Me	4-^{t}BuC_6H_4	53	89	(2*R*,3*S*)[d]
23	AnBOX	**2j**	H	*trans*-4-Pr-*c*C_6H_{10}	54	20	(2*S*,3*R*)[d]
24	BOX	*ent*-**2j**	H	*trans*-4-Pr-*c*C_6H_{10}	9	30	(2*R*,3*S*)[d]
25	*S*-*c*HBOX	**2j**	H	*trans*-4-Pr-*c*C_6H_{10}	9	48	(2*S*,3*R*)[d]
26	AnBOX	**2k**	H	Me	65	50[c]	(2*S*,3*R*)
27	BOX	*ent*-**2k**	H	Me	15	85	(2*R*,3*S*)
28	*S*-*c*HBOX	*rac*-**2k**	H	Me	37	0	

[a] Isolated yields after the silica gel column chromatography.
[b] Determined by HPLC analysis with chiral column (4.6 × 250 mm, Chiralpak).
[c] Determined by comparing the measured specific rotation with the reported one.[13,15]
[d] Determined tentatively on the basis of the same mechanism and transition state.



Scheme 1. The structures of AnBOX, BOX, and *S*-*c*HBOX ligands.

transition state in the catalytic asymmetric aziridination (Fig. 1).[13]

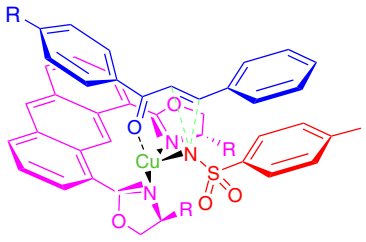


Figure 1. π-Stacking interaction between AnBOX and chalcones in the transition state in the asymmetric aziridination.

To verify this assumption, we prepared three chalcones **1g**–**1i** with 4′-branched isopropyl and *tert*-butyl groups, which could disrupt the formation of the ligand–substrate attractive aromatic π-stacking interaction due to bulky steric hindrance. These were aziridinated asymmetrically under the catalysis of AnBOX, BOX, and (*S*)-*c*HBOX, respectively. The results are summarized in Table 1 (entries 14–22). The results clearly indicate that the AnBOX ligand gives relatively lower enantioselectivity for these three chalcones in comparison with 4′-methylchalcone due to little π-stacking interaction effectively (entries 1, 14, 17, and 20). However, BOX and (*S*)-*c*HBOX ligands still show high enantioselectivities for these three chalcones as for 4′-methylchalcone (entries 1, 15, 16, 18, 19, 21, and 22).

To further confirm our rationale, 1-(*trans*-4-propylcyclohexyl)-3-phenyl-2-propen-1-one **1j** and 4-phenyl-but-3-en-2-one **1k** were asymmetrically aziridinated under the action of these three catalysts. The results indicate that lower enantioselectivities were obtained under the catalysis of AnBOX because of no π-stacking interaction between the ligand and substrates, due to the absence of a phenyl group attached to the carbonyl group in substrates. These results also support our rationale.

Although these three ligands are somewhat different in terms of bite angle, the inter-N-heteroatom distance, and disposition of chirality, ligands AnBOX and (*S*)-*c*HBOX possess similar chiral environments. It is impossible to design and synthesize two ligands with identical chiral environments; one with an aromatic backbone and the other with aliphatic backbone. However, ligands have similar structural features.

The origin of the π-stacking interaction has been investigated experimentally and theoretically.[17] The results indicate that the π-stacking interaction is a complex interaction, including charge transfer (also called π-acid/base), van der Vaals (dispersive), and polar electrostatic (Coulombic) components.[18] The AnBOX ligand shows higher enantioselectivity with electron-rich chalcones than with electron-deficient chalcones.[13] It seems reasonable to consider the anthracene ring in AnBOX as a relatively electron-deficient aromatic system as it possesses two electron-withdrawing oxazolin-2-yl groups. The substituent-dependent enantioselectivity could be rationalized to the stabilization generated from the charge-transfer complexation between the ligand–substrate aromatic π-stacking interaction in the transition state. Electron-rich chalcones show more obvious charge-transfer complexation with the ligand than electron-deficient ones. Thus, their ligand–substrate aromatic π-stacking interaction in the transition state is more stable than that between the anthracene ring and electron-deficient chalcones. These can reduce the conformational degrees of freedom and enhance the chiral discrimination in the selectivity-determining transition state via the ligand–substrate attractive aromatic π-stacking interaction.

On the basis of our proposed transition state (Fig. 1),[13] if chalcones form a stable π-stacking complex, they will undergo stereospecific aziridination from the upper face of the chalcones to afford (2*S*,3*R*)-aziridine products due to π-shielding (the same products should be obtained from the bottom due to C_2-symmetric ligand). The racemic products should be obtained from a non-catalytic pathway. Thus, the enantiomeric excesses should present the percents of chalcones that formed stable π-stacking complex with AnBOX. The stability should be related to the Hammett constants because both the stability and the Hammett constants are related to the electronic density of the aromatic rings of chalcones. The ee values and Hammett constants show a satisfactory correlation (Fig. 2). This further indicates that the π-stacking interaction is predominant in the charge-transfer interaction between the ligand and substrates. The enantioselective catalytic reaction provides a sensitive probe to investigate weak intermolecular interactions, such as π-stacking interaction.

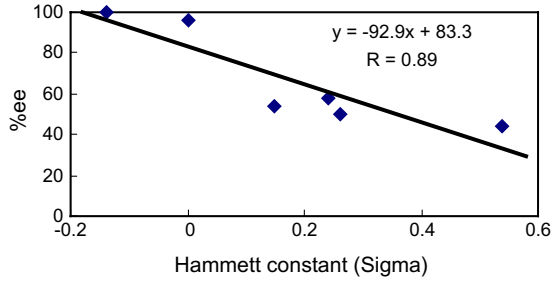


Figure 2. Hammett plot of the enantiomeric excesses versus Hammett constants in the AnBOX catalyzed aziridination of chalcones.

To further confirm our rationale, we attempted to prepare modified AnBOX with electron-rich substituents (such as Me, MeO, Me_2N) on its anthracene backbone and hoped to observe a positive slope in the corresponding Hammett

plot. Unfortunately, we failed in the synthesis of the designed AnBOX ligands.

3. Conclusion

In conclusion, factors governing enantioselectivity in the catalytic asymmetric reaction are usually interpreted in steric terms of catalysts, affected by the temperature and solvent, etc.[19] Recently, much attention has been paid to the influence of electronic effects on the enantioselectivity in the asymmetric catalysis.[20–22] However, the underlying reasons are poorly understood in the most cases. Our results indicate that the origin of the substituent-dependent enantioselectivity in the asymmetric aziridination of chalcones catalyzed by AnBOX is the π-stacking interaction between the ligand backbone and substrates. The results also indicate that the π-stacking interaction between the ligand backbone and substrates is one of more important factors for controlling the enantioselectivity in asymmetric catalysis. The results provide very useful information for understanding the influence of the electronic effect of catalysts possessing aromatic backbones or substituents on aromatic substrates and for designing novel ligands. The results also reveal that the enantioselective catalytic reaction provides a sensitive probe to investigate weak intermolecular interactions, such as π-stacking interaction.

4. Experimental

4.1. General method

Melting points were measured on a Yanaco MP-500 melting point apparatus and are uncorrected. IR spectra were recorded on a Bruker Vector 22 FT IR spectrophotometer, ^{1}H NMR and ^{13}C NMR spectra were on a Varian Mercury 200 (200 MHz) or Varian Mercury Plus 300 (300 MHz) spectrometer in $CDCl_3$ solution with TMS as an internal standard while chemical shifts are reported in parts per million. Low and high resolution mass spectra were obtained on a VG-ZAB-HS spectrometer. CH analyses were performed on an Elementar Vario EL analyzer. Optical rotations were measured on a Perkin Elmer Model 341LC polarimeter with a thermally jacketed 10 cm cell (concentration c expressed as g/100 mL). The ee values were determined by HPLC analysis on an HP1100 HPLC equipment with chiral columns (4.6 × 250 mm) applying a mixture of hexane–isopropanol as an eluent. Dichloromethane was heated at reflux over calcium hydride and distilled prior to use.

4.2. General procedure for the synthesis of unsaturated ketones 1f–j

To a stirred solution of the aldehyde (10 mmol) and ketone (10 mmol) in 5 mL of ethanol was added 2.5 mL of 10% NaOH at 0 °C. After this addition, the ice-bath was removed and the mixture allowed to warm to room temperature and stirred for 1 h. After filtration, a yellow solid was obtained as crude unsaturated ketone. The solid was recrystallized from EtOH to give yellow crystals. Analytical data of all the known unsaturated ketones are identical to the reported ones.[23]

4.2.1. (*E*)-1-(4-*tert*-Butylphenyl)-3-(4-methylphenyl)-2-propen-1-one 1i.[24] Yellow needle crystals, yield 70%; mp 110–112 °C; R_f 0.53 [ethyl acetate–petroleum ether (60–90 °C) 1:8 (v/v), silica gel plate]. IR (KBr) ν (cm^{-1}): 1667 (s); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.36 (s, 9H), 2.39 (s, 3H), 7.22 (d, $J = 8.0$ Hz, 2H), 7.46–7.56 (m, 5H), 7.79 (d, $J = 15.6$ Hz, 1H), 7.97 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 21.5, 31.1, 35.1, 121.1, 125.5, 128.4, 129.6, 132.2, 135.6, 140.9, 144.4, 156.4, 190.1. MS (EI) m/z: 278 (M^+); Anal. Calcd for $C_{20}H_{22}O$: C, 86.29; H, 7.97. Found: C, 85.98; H, 8.09.

4.2.2. (*E*)-3-Phenyl-1-(*trans*-4-propylcyclohexyl)-2-propen-1-one 1j. Yellow crystals, yield 77%; mp 43–45 °C; R_f 0.72 [ethyl acetate–petroleum ether (60–90 °C) 1:8 (v/v), silica gel plate]. IR (KBr) ν (cm^{-1}): 1680 (s); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.89 (d, $J = 7.2$ Hz, 3H), 0.98 (q, $J = 7.2$ Hz, 2H), 1.15–1.50 (m, 7H), 2.60 (m, 1H), 6.81 (d, $J = 16.0$ Hz, 1H), 7.32–7.58 (m, 5H), 7.59 (d, $J = 16.0$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.3, 19.8, 28.6, 32.3, 36.7, 39.5, 49.5, 124.7, 128.2, 128.8, 130.2, 134.6, 142.1, 203.2. MS (EI) m/z: 256 (M^+); Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.18; H, 9.26.

4.3. General procedure for the asymmetric aziridination of chalcones

A three-necked flask (25 mL) was charged with α,β-unsaturated ketone **1** (1.50 mmol), ligand (0.06 mmol), and CuOTf·1/2C_6H_6 (13 mg, 0.05 mmol) under a nitrogen atmosphere. Dichloromethane (8 mL) was added by syringe and the resulting mixture was stirred for 1 h at 24 °C. PhI=NTs (373 mg, 1.00 mmol) was added portionwise to the mixture over 2 h. After the addition, the reaction mixture was kept stirring for another 3 h. The aziridine product was obtained after flash silica gel chromatography with a mixture of petroleum ether (60–90 °C) and ethyl acetate (6:1, v/v) as an eluent.

4.3.1. (2*S*,3*R*)-3-Phenyl-2-(4-trifluoromethylbenzoyl)-1-(*p*-tolylsulfonyl)aziridine 2f. Colorless crystals, yield 70%; mp 135–137 °C; R_f 0.48 [ethyl acetate–petroleum ether (60–90 °C) 1:5 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OD-H column with hexane–2-propanol (97:3, v/v) as an eluent at flow rate 1.0 mL/min ($\tau_{major} = 41.6$ min; $\tau_{minor} = 46.2$ min): $[\alpha]_D^{16} = +8.85$ (c 0.87, $CHCl_3$, 44% ee); IR (KBr) ν (cm^{-1}): 1702 (s), 1326 (s), 1161 (s); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.40 (s, 3H), 4.20 (d, $J = 4.0$ Hz, 1H), 4.57 (d, $J = 4.0$ Hz, 1H), 7.22–7.34 (m, 7H), 7.68–7.76 (m, 4H), 8.16 (d, $J = 7.8$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 21.7, 47.0, 50.5, 125.8, 125.9, 127.5, 127.7, 128.6, 129.0, 129.3, 129.5, 132.8, 136.4, 138.5, 144.5, 189.7; MS (EI) m/z (relative intensity, %): 445 (M^+, 4.1), 290 (100), 173 (97), 145 (26), 91 (17); Anal. Calcd for $C_{23}H_{18}F_3NO_3S$: C, 62.01; H, 4.07; N, 3.14. Found: C, 61.95; H, 4.09; N, 3.01.

4.3.2. (2*R*,3*S*)-3-Phenyl-2-(4-trifluoromethylbenzoyl)-1-(*p*-tolylsulfonyl)aziridine *ent*-2f. Colorless crystals, yield 4%; mp 141–143 °C; R_f 0.48 [ethyl acetate–petroleum ether (60–90 °C) 1:5 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OD-H column with hexane–2-propanol (97:3, v/v) as an eluent at flow rate 1.0 mL/min ($\tau_{minor} = 41.6$ min; $\tau_{major} = 45.7$ min): $[\alpha]_D^{16} = -13.9$ (*c* 1.0, $CHCl_3$, 65% ee); IR (KBr) *v* (cm^{-1}): 1701 (s), 1326 (s), 1163 (s); ^1H NMR (200 MHz, $CDCl_3$) δ: 2.41 (s, 3H), 4.20 (d, $J = 4.0$ Hz, 1H), 4.57 (d, $J = 4.0$ Hz, 1H), 7.24–7.34 (m, 7H), 7.69–7.76 (m, 4H), 8.16 (d, $J = 7.8$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 21.6, 47.0, 50.4, 125.76, 125.84, 127.3, 127.7, 128.7, 129.0, 129.3, 129.6, 132.8, 136.2, 138.5, 144.7, 189.7; MS (EI) *m*/*z* (relative intensity, %): 445 (M^+, 4), 290 (100), 173 (97), 145 (26), 91 (17); Anal. Calcd for $C_{23}H_{18}F_3NO_3S$: C, 62.01; H, 4.07; N, 3.14. Found: C, 61.99; H, 4.00; N, 3.05.

4.3.3. (2*S*,3*R*)-2-(4-Isopropylbenzoyl)-3-phenyl-1-(*p*-tolylsulfonyl)aziridine 2g. Colorless crystals, yield 72%; mp 106–108 °C; R_f 0.32 [ethyl acetate–petroleum ether (60–90 °C) 1:8 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OD-H column with hexane–2-propanol (90:10, v/v) as an eluent at flow rate 0.8 mL/min ($\tau_{major} = 16.9$ min; $\tau_{minor} = 21.5$ min): $[\alpha]_D^{20} = +5.7$ (*c* 0.80, $CHCl_3$, 66% ee); IR (KBr) *v* (cm^{-1}): 1685 (s), 1332 (s), 1162 (s); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.27 (d, $J = 6.9$ Hz, 6H), 2.39 (s, 3H), 2.98 (heptet, $J = 6.9$ Hz, 1H), 4.29 (d, $J = 4.2$ Hz, 1H), 4.52 (d, $J = 4.2$ Hz, 1H), 7.20–7.24 (m, 2H), 7.33–7.36 (m, 7H), 7.71–7.75 (m, 2H), 7.98–8.00 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 21.6, 23.7, 23.6, 34.3, 47.6, 50.1, 126.9, 127.4, 127.7, 128.6, 128.8, 129.1, 129.4, 132.9, 133.8, 136.6, 144.4, 155.8, 189.9; MS (EI) *m*/*z* (relative intensity, %): 419 (M^+, 1.5), 264 (100), 248 (61), 209 (53), 147 (93), 91 (49); HRMS Calcd for $C_{25}H_{25}NO_3S$: 419.1555. Found: 419.1556.

4.3.4. (2*R*,3*S*)-2-(4-Isopropylbenzoyl)-3-phenyl-1-(*p*-tolylsulfonyl)aziridine *ent*-2g. Colorless crystals, yield 24%; mp 106–108 °C; R_f 0.32 [ethyl acetate–petroleum ether (60–90 °C) 1:8 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OD-H column with hexane–2-propanol (90:10, v/v) as an eluent at flow rate 0.8 mL/min ($\tau_{minor} = 17.2$ min; $\tau_{major} = 21.7$ min): $[\alpha]_D^{20} = -7.29$ (*c* 1.00, $CHCl_3$, 85% ee); IR (KBr) *v* (cm^{-1}): 1685 (s), 1332 (s), 1162 (s); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.28 (d, $J = 6.9$ Hz, 6H), 2.39 (s, 3H), 2.98 (heptet, $J = 6.9$ Hz, 1H), 4.29 (d, $J = 4.2$ Hz, 1H), 4.51 (d, $J = 4.2$ Hz, 1H), 7.21–7.24 (m, 2H), 7.32–7.37 (m, 7H), 7.71–7.74 (m, 2H), 7.99–8.01 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 21.6, 23.5, 23.6, 34.3, 47.4, 50.1, 126.9, 127.5, 127.7, 128.6, 128.8, 129.2, 129.4, 132.9, 133.8, 136.6, 144.2, 155.8, 189.7; MS (EI) *m*/*z* (relative intensity, %): 419 (M^+, 2), 264 (100), 248 (60), 209 (53), 147 (91), 91 (49); HRMS Calcd for $C_{25}H_{25}NO_3S$: 419.1555. Found: 419.1554.

4.3.5. (2*S*,3*R*)-2-(4-*tert*-Butylbenzoyl)-3-phenyl-1-(*p*-tolylsulfonyl)aziridine 2h. Colorless crystals, yield 79%; mp 122–124 °C; R_f 0.37 [ethyl acetate–petroleum ether (60–90 °C) 1:6 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OD-H column with hexane–2-propanol (90:10, v/v) as an eluent at flow rate 0.8 mL/min ($\tau_{major} = 16.8$ min; $\tau_{minor} = 20.0$ min): $[\alpha]_D^{20} = +5.1$ (*c* 0.81, $CHCl_3$, 70% ee); IR (KBr) *v* (cm^{-1}): 1689 (s), 1333 (s), 1162 (s); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.34 (s, 9H), 2.40 (s, 3H), 4.25 (d, $J = 4.2$ Hz, 1H), 4.51 (d, $J = 4.2$ Hz, 1H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.33 (m, 5H), 7.45 (d, $J = 8.7$ Hz, 2H), 7.72 (d, $J = 8.1$ Hz, 2H), 7.96 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 21.7, 31.0, 35.3, 47.4, 50.1, 125.8, 127.8, 128.6, 128.8, 128.9, 129.4, 132.7, 133.4, 136.6, 144.1, 158.0, 189.6; MS (EI) *m*/*z* (relative intensity, %): 433 (M^+, 2.9), 278 (19), 277 (30), 262 (46), 161 (100), 91 (35); Anal. Calcd for $C_{26}H_{27}NO_3S$: C, 72.03; H, 6.28; N, 3.23. Found: C, 70.91; H, 6.23; N, 3.01.

4.3.6. (2*R*,3*S*)-2-(4-*tert*-Butylbenzoyl)-3-phenyl-1-(*p*-tolylsulfonyl)aziridine *ent*-2h. Colorless crystals, yield 43%; mp 121–123 °C; R_f 0.37 [ethyl acetate–petroleum ether (60–90 °C) 1:6 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OD-H column with hexane–2-propanol (90:10, v/v) as an eluent at flow rate 0.8 mL/min ($\tau_{minor} = 16.6$ min; $\tau_{major} = 19.2$ min): $[\alpha]_D^{20} = -6.1$ (*c* 0.66, $CHCl_3$, 98% ee); IR (KBr) *v* (cm^{-1}): 1688 (s), 1333 (s), 1163 (s); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.35 (s, 9H), 2.40 (s, 3H), 4.25 (d, $J = 4.2$ Hz, 1H), 4.51 (d, $J = 4.2$ Hz, 1H), 7.23 (d, $J = 8.1$ Hz, 2H), 7.36 (m, 5H), 7.45 (d, $J = 8.7$ Hz, 2H), 7.72 (d, $J = 8.1$ Hz, 2H), 7.95 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 21.6, 31.0, 35.3, 47.4, 50.1, 125.8, 127.6, 128.6, 128.8, 128.9, 129.4, 132.9, 133.4, 136.6, 144.3, 158.0, 189.8; MS (EI) *m*/*z* (relative intensity, %): 433 (M^+, 3), 278 (19), 277 (30), 262 (44), 161 (100), 91 (34); Anal. Calcd for $C_{26}H_{27}NO_3S$: C, 72.03; H, 6.28; N, 3.23. Found: C, 70.95; H, 6.20; N, 3.12.

4.3.7. (2*S*,3*R*)-2-(4-*tert*-Butylbenzoyl)-3-tolyl-1-(*p*-tolylsulfonyl)aziridine 2i. Colorless crystals, yield 86%; mp 129–130 °C; R_f 0.28 [ethyl acetate–petroleum ether (60–90 °C) 1:6 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OD-H column with hexane–2-propanol (90:10, v/v) as an eluent at flow rate 0.8 mL/min ($\tau_{major} = 15.5$ min; $\tau_{minor} = 17.2$ min): $[\alpha]_D^{20} = -3.42$ (*c* 0.76, $CHCl_3$, 71% ee); IR (KBr) *v* (cm^{-1}): 1685 (s), 1332 (s), 1162 (s); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.35 (s, 9H), 2.35 (s, 3H), 2.39 (s, 3H), 4.35 (d, $J = 4.2$ Hz, 1H), 4.45 (d, $J = 4.2$ Hz, 1H), 7.15 (d, $J = 7.8$ Hz, 2H), 7.20–7.25 (m, 4H), 7.49 (d, $J = 9.0$ Hz, 2H), 7.73 (d, $J = 8.4$ Hz, 2H), 7.98 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 21.2, 21.7, 31.2, 35.2, 47.8, 49.7, 125.7, 127.6, 127.7, 128.8, 129.3, 129.4, 129.6, 133.4, 136.9, 138.8, 144.3, 158.0, 190.2; MS (EI) *m*/*z* (relative intensity, %): 447 (M^+, 0.21), 292 (17), 291 (67), 276 (100), 248 (10), 91 (33); Anal. Calcd for $C_{27}H_{29}NO_3S$: C, 72.45; H, 6.53; N, 3.13. Found: C, 72.41; H, 6.56; N, 2.99.

4.3.8. (2*R*,3*S*)-2-(4-*tert*-Butylbenzoyl)-3-tolyl-1-(*p*-tolylsulfonyl)aziridine *ent*-2i. Colorless crystals, yield 53%; mp 131–133 °C; R_f 0.28 [ethyl acetate–petroleum ether (60–90 °C) 1:6 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OD-H column with

hexane–2-propanol (90:10, v/v) as an eluent at flow rate 0.8 mL/min ($\tau_{minor} = 15.1$ min; $\tau_{major} = 16.2$ min): $[\alpha]_D^{20} = +4.6$ (*c* 0.65, $CHCl_3$, 89% ee); IR (KBr) *v* (cm^{-1}): 1685 (s), 1331 (s), 1163 (s); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.35 (s, 9H), 2.35 (s, 3H), 2.39 (s, 3H), 4.34 (d, $J = 4.2$ Hz, 1H), 4.45 (d, $J = 4.2$ Hz, 1H), 7.15 (d, $J = 7.8$ Hz, 2H), 7.21–7.27 (m, 4H), 7.49 (d, $J = 9.0$ Hz, 2H), 7.73 (d, $J = 8.4$ Hz, 2H), 7.99 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 21.2, 21.6, 31.0, 35.2, 47.8, 49.7, 125.7, 127.6, 127.7, 128.8, 129.3, 129.4, 129.6, 133.4, 136.8, 138.8, 144.2, 158.0, 190.0; MS (EI) *m*/*z* (relative intensity, %): 447 (M^+, 0.5), 292 (17), 291 (69), 276 (100), 248 (11), 91 (35); Anal. Calcd for $C_{27}H_{29}NO_3S$: C, 72.45; H, 6.53; N, 3.13. Found: C, 72.39; H, 6.50; N, 3.03.

4.3.9. (2*S*,3*R*)-3-Phenyl-2-(*trans*-4-propylcyclohexylformyl)-1-(*p*-tolylsulfonyl)aziridine 2j. Colorless crystals, yield 9%; mp 135–137 °C; R_f 0.33 [ethyl acetate–petroleum ether (60–90 °C) 1:10 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OJ-H column with hexane–2-propanol (90:10, v/v) as an eluent at flow rate 0.8 mL/min ($\tau_{major} = 23.9$ min; $\tau_{minor} = 37.2$ min): $[\alpha]_D^{20} = +5.05$ (*c* 1.00, $CHCl_3$, 48% ee); IR (KBr) *v* (cm^{-1}): 1716 (s), 1334 (s), 1163 (s); ^1H NMR (300 MHz, $CDCl_3$) δ: 0.86–0.96 (m, 5H), 1.13–1.45 (m, 7H), 1.76–2.00 (m, 4H), 2.41 (s, 3H), 2.56–2.60 (m, 1H), 3.77 (d, $J = 4.2$ Hz, 1H), 4.27 (d, $J = 4.2$ Hz, 1H), 7.24–7.33 (m, 7H), 7.74 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.3, 19.9, 21.6, 27.6, 28.2, 32.1, 32.2, 36.6, 39.4, 48.9, 49.9, 50.2, 127.5, 127.9, 128.5, 128.9, 129.5, 132.2, 137.1, 144.2, 204.9; MS (EI) *m*/*z* (relative intensity, %): 425 (M^+, 3.0), 270 (100), 118 (65), 91 (75); Anal. Calcd for $C_{25}H_{31}NO_3S$: C, 70.55; H, 7.34; N, 3.29. Found: C, 70.55; H, 7.20; N, 3.03.

4.3.10. (2*R*,3*S*)-3-Phenyl-2-(*trans*-4-propylcyclohexylformyl)-1-(*p*-tolylsulfonyl)aziridine *ent*-2j. Colorless crystals, yield 9%; mp 130–132 °C; R_f 0.33 [ethyl acetate–petroleum ether (60–90 °C) 1:10 (v/v), silica gel plate]; The ee value was determined by HPLC with Chiralcel OJ-H column with hexane–2-propanol (90:10, v/v) as an eluent at flow rate 0.8 mL/min ($\tau_{minor} = 24.0$ min; $\tau_{major} = 39.0$ min): $[\alpha]_D^{20} = -3.0$ (*c* 1.00, $CHCl_3$, 30% ee); IR (KBr) *v* (cm^{-1}): 1717 (s), 1332 (s), 1161 (s); ^1H NMR (300 MHz, $CDCl_3$) δ: 0.85–0.96 (m, 5H), 1.13–1.46 (m, 7H), 1.78–2.00 (m, 4H), 2.41 (s, 3H), 2.55–2.60 (m, 1H), 3.78 (d, $J = 4.2$ Hz, 1H), 4.27 (d, $J = 4.2$ Hz, 1H), 7.25–7.34 (m, 7H), 7.73 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.3, 19.8, 21.6, 27.6, 28.1, 32.1, 32.2, 36.6, 39.4, 48.9, 49.9, 50.2, 127.5, 127.8, 128.5, 128.9, 129.5, 132.2, 137.0, 144.3, 204.9; MS (EI) *m*/*z* (relative intensity, %): 425 (M^+, 3.0), 270 (100), 118 (67), 91 (76); Anal. Calcd for $C_{25}H_{31}NO_3S$: C, 70.55; H, 7.34; N, 3.29. Found: C, 70.58; H, 7.21; N, 3.12.

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